

=> d his

(FILE 'HOME' ENTERED AT 14:34:31 ON 25 FEB 2003)

FILE 'CA' ENTERED AT 14:35:50 ON 25 FEB 2003
S 130170-60-4/REG#

L1 FILE 'REGISTRY' ENTERED AT 14:36:19 ON 25 FEB 2003
1 S 130170-60-4/RN

L2 FILE 'CA' ENTERED AT 14:36:20 ON 25 FEB 2003
1 S L1
S 130370-60-4/REG#

L3 FILE 'REGISTRY' ENTERED AT 14:36:52 ON 25 FEB 2003
1 S 130370-60-4/RN

L4 FILE 'CA' ENTERED AT 14:36:52 ON 25 FEB 2003
169 S L3
E WO 98/23588/PN 25
E WO 9823588/PN 25

L5 1 S E3
L6 0 S L5 AND L4
E US5763621/PN 25
L7 1 S E3
L8 0 S L7 AND L4

FILE 'HOME' ENTERED AT 14:40:45 ON 25 FEB 2003

FILE 'REGISTRY' ENTERED AT 14:42:09 ON 25 FEB 2003

L9 FILE 'CA' ENTERED AT 14:42:12 ON 25 FEB 2003
65 S (BRITISH BIOTECH)/PA
L10 2 S L9 AND L4
L11 1 (HYDROXAMIC ACID BASED COLLAGENASE INHIBITORS)/TI
E WO9005719/PN 25
L12 1 S E3

L13 FILE 'MEDLINE' ENTERED AT 14:55:18 ON 25 FEB 2003
17565 S NEOVASCULARIZATION
L14 19592 S RETINOPATHY
L15 35854 S L13 OR L14
L16 301 S BATIMASTAT OR BB94 OR (BB 94)
L17 27 S L16 AND L15

L18 FILE 'WPIDS' ENTERED AT 15:01:28 ON 25 FEB 2003
2 S L17

L19 FILE 'CA' ENTERED AT 15:02:08 ON 25 FEB 2003
7 S L18

=> log hold

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	34.47	148.46
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	-3.72	-6.20

SESSION WILL BE HELD FOR 60 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 15:15:08 ON 25 FEB 2003

=> d his

(FILE 'HOME' ENTERED AT 14:34:31 ON 25 FEB 2003)

FILE 'CA' ENTERED AT 14:35:50 ON 25 FEB 2003
S 130170-60-4/REG#

L1 FILE 'REGISTRY' ENTERED AT 14:36:19 ON 25 FEB 2003
1 S 130170-60-4/RN

L2 FILE 'CA' ENTERED AT 14:36:20 ON 25 FEB 2003
1 S L1
S 130370-60-4/REG#

L3 FILE 'REGISTRY' ENTERED AT 14:36:52 ON 25 FEB 2003
1 S 130370-60-4/RN

L4 FILE 'CA' ENTERED AT 14:36:52 ON 25 FEB 2003
169 S L3
E WO 98/23588/PN 25
E WO 9823588/PN 25

L5 1 S E3
L6 0 S L5 AND L4
E US5763621/PN 25
L7 1 S E3
L8 0 S L7 AND L4

FILE 'HOME' ENTERED AT 14:40:45 ON 25 FEB 2003

FILE 'REGISTRY' ENTERED AT 14:42:09 ON 25 FEB 2003

L9 FILE 'CA' ENTERED AT 14:42:12 ON 25 FEB 2003
65 S (BRITISH BIOTECH)/PA
L10 2 S L9 AND L4
L11 1 (HYDROXAMIC ACID BASED COLLAGENASE INHIBITORS)/TI
E WO9005719/PN 25
L12 1 S E3

L13 FILE 'MEDLINE' ENTERED AT 14:55:18 ON 25 FEB 2003
17565 S NEOVASCULARIZATION
L14 19592 S RETINOPATHY
L15 35854 S L13 OR L14
L16 301 S BATIMASTAT OR BB94 OR (BB 94)
L17 27 S L16 AND L15

L18 FILE 'WPIDS' ENTERED AT 15:01:28 ON 25 FEB 2003
2 S L17

L19 FILE 'CA' ENTERED AT 15:02:08 ON 25 FEB 2003
7 S L18

L20 FILE 'BIOSIS' ENTERED AT 15:56:27 ON 25 FEB 2003
2555 S (DRUGS FUTURE)/SO
L21 229 S BATIMASTAT
L22 567195 S PD=1997
L23 13 S L22 AND L21
L24 251 S PTERYGIA
L25 229 S BATIMASTAT
L26 0 S L24 AND L25

L27 FILE 'MEDLINE' ENTERED AT 16:05:22 ON 25 FEB 2003
0 S L26

FILE 'CA' ENTERED AT 16:05:45 ON 25 FEB 2003

L28 1 S L27

FILE 'ADISCTI, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, AQUASCI, BIOBUSINESS, BIOCOMMERCE, BIOSIS, BIOTECHDS, BIOTECHNO, CABA, CANCERLIT, CAPLUS, CEABA-VTB, CEN, CIN, CONFSCI, CROPB, CROPU, DGENE, DRUGB, DRUGLAUNCH, DRUGMONOG2, DRUGNL, DRUGU, DRUGUPDATES, ...' ENTERED AT 16:06:08 ON 25 FEB 2003

L29	61	FILE ADISCTI
L30	8	FILE ADISINSIGHT
L31	4	FILE ADISNEWS
L32	0	FILE AGRICOLA
L33	0	FILE ANABSTR
L34	0	FILE AQUASCI
L35	19	FILE BIOBUSINESS
L36	25	FILE BIOCOMMERCE
L37	229	FILE BIOSIS
L38	0	FILE BIOTECHDS
L39	168	FILE BIOTECHNO
L40	2	FILE CABA
L41	109	FILE CANCERLIT
L42	208	FILE CAPLUS
L43	14	FILE CEABA-VTB
L44	0	FILE CEN
L45	37	FILE CIN
L46	3	FILE CONFSCI
L47	0	FILE CROPB
L48	0	FILE CROPU
L49	0	FILE DGENE
L50	0	FILE DRUGB
L51	0	FILE DRUGLAUNCH
L52	0	FILE DRUGMONOG2
L53	19	FILE DRUGNL
L54	165	FILE DRUGU
L55	2	FILE DRUGUPDATES
L56	4	FILE EMBAL
L57	478	FILE EMBASE
L58	129	FILE ESBIODBASE
L59	1	FILE FEDRIP
L60	0	FILE FOMAD
L61	0	FILE FOREGE
L62	0	FILE FROSTI
L63	0	FILE FSTA
L64	0	FILE GENBANK
L65	0	FILE HEALSAFE
L66	14	FILE IFIPAT
L67	6	FILE JICST-EPLUS
L68	0	FILE KOSMET
L69	22	FILE LIFESCI
L70	0	FILE MEDICNF
L71	163	FILE MEDLINE
L72	0	FILE NIOSHTIC
L73	0	FILE NTIS
L74	0	FILE NUTRACEUT
L75	0	FILE OCEAN
L76	110	FILE PASCAL
L77	4	FILE PHAR
L78	46	FILE PHARMAML
L79	0	FILE PHIC
L80	67	FILE PHIN
L81	114	FILE PROMT
L82	235	FILE SCISEARCH
L83	1	FILE SYNTHLINE
L84	150	FILE TOXCENTER

L85	162	FILE	USPATFULL
L86	12	FILE	USPAT2
L87	0	FILE	VETB
L88	0	FILE	VETU
L89	13	FILE	WPIDS
TOTAL FOR ALL FILES			
L90	2804	S	BATIMASTAT
L91	5	FILE	ADISCTI
L92	1	FILE	ADISINSIGHT
L93	0	FILE	ADISNEWS
L94	0	FILE	AGRICOLA
L95	0	FILE	ANABSTR
L96	0	FILE	AQUASCI
L97	2	FILE	BIOBUSINESS
L98	2	FILE	BIOCOMMERCE
L99	251	FILE	BIOSIS
L100	1	FILE	BIOTECHDS
L101	21	FILE	BIOTECHNO
L102	0	FILE	CABA
L103	54	FILE	CANCERLIT
L104	18	FILE	CAPLUS
L105	1	FILE	CEABA-VTB
L106	0	FILE	CEN
L107	1	FILE	CIN
L108	4	FILE	CONFSCI
L109	0	FILE	CROPB
L110	0	FILE	CROPU
L111	77	FILE	DGENE
L112	1	FILE	DRUGB
L113	0	FILE	DRUGLAUNCH
L114	0	FILE	DRUGMONOG2
L115	2	FILE	DRUGNL
L116	7	FILE	DRUGU
L117	1	FILE	DRUGUPDATES
L118	3	FILE	EMBAL
L119	288	FILE	EMBASE
L120	28	FILE	ESBIOBASE
L121	0	FILE	FEDRIP
L122	0	FILE	FOMAD
L123	0	FILE	FOREGE
L124	0	FILE	FROSTI
L125	0	FILE	FSTA
L126	0	FILE	GENBANK
L127	1	FILE	HEALSAFE
L128	0	FILE	IFIPAT
L129	15	FILE	JICST-EPLUS
L130	0	FILE	KOSMET
L131	12	FILE	LIFESCI
L132	0	FILE	MEDICONF
L133	317	FILE	MEDLINE
L134	4	FILE	NIOSHTIC
L135	0	FILE	NTIS
L136	0	FILE	NUTRACEUT
L137	1	FILE	OCEAN
L138	133	FILE	PASCAL
L139	2	FILE	PHAR
L140	1	FILE	PHARMAML
L141	0	FILE	PHIC
L142	3	FILE	PHIN
L143	20	FILE	PROMT
L144	248	FILE	SCISEARCH
L145	0	FILE	SYNTHLINE
L146	86	FILE	TOXCENTER
L147	120	FILE	USPATFULL

L148	1	FILE	USPAT2
L149	0	FILE	VETB
L150	0	FILE	VETU
L151	4	FILE	WPIDS
TOTAL FOR ALL FILES			
L152	1736	S	PTERYGIA
L153	0	FILE	ADISCTI
L154	1	FILE	ADISINSIGHT
L155	0	FILE	ADISNEWS
L156	0	FILE	AGRICOLA
L157	0	FILE	ANABSTR
L158	0	FILE	AQUASCI
L159	1	FILE	BIOBUSINESS
L160	0	FILE	BIOCOMMERCE
L161	0	FILE	BIOSIS
L162	0	FILE	BIOTECHDS
L163	0	FILE	BIOTECHNO
L164	0	FILE	CABA
L165	0	FILE	CANCERLIT
L166	1	FILE	CAPLUS
L167	1	FILE	CEABA-VTB
L168	0	FILE	CEN
L169	1	FILE	CIN
L170	0	FILE	CONFSCI
L171	0	FILE	CROPB
L172	0	FILE	CROPU
L173	0	FILE	DGENE
L174	0	FILE	DRUGB
L175	0	FILE	DRUGLAUNCH
L176	0	FILE	DRUGMONOG2
L177	2	FILE	DRUGNL
L178	0	FILE	DRUGU
L179	1	FILE	DRUGUPDATES
L180	0	FILE	EMBAL
L181	0	FILE	EMBASE
L182	0	FILE	ESBIOBASE
L183	0	FILE	FEDRIP
L184	0	FILE	FOMAD
L185	0	FILE	FOREGE
L186	0	FILE	FROSTI
L187	0	FILE	FSTA
L188	0	FILE	GENBANK
L189	0	FILE	HEALSAFE
L190	0	FILE	IFIPAT
L191	0	FILE	JICST-EPLUS
L192	0	FILE	KOSMET
L193	0	FILE	LIFESCI
L194	0	FILE	MEDICONF
L195	0	FILE	MEDLINE
L196	0	FILE	NIOSHTIC
L197	0	FILE	NTIS
L198	0	FILE	NUTRACEUT
L199	0	FILE	OCEAN
L200	0	FILE	PASCAL
L201	2	FILE	PHAR
L202	1	FILE	PHARMAML
L203	0	FILE	PHIC
L204	0	FILE	PHIN
L205	3	FILE	PROMT
L206	0	FILE	SCISEARCH
L207	0	FILE	SYNTHLINE
L208	1	FILE	TOXCENTER
L209	0	FILE	USPATFULL
L210	0	FILE	USPAT2

L211 0 FILE VETB
L212 0 FILE VETU
L213 0 FILE WPIDS
 TOTAL FOR ALL FILES
L214 15 S L90 AND L152

FILE 'STNGUIDE' ENTERED AT 16:12:21 ON 25 FEB 2003

FILE 'PROMT' ENTERED AT 16:16:19 ON 25 FEB 2003

L215 1 S 97:455776/AN

=>

> d his

(FILE 'HOME' ENTERED AT 12:49:29 ON 25 FEB 2003)

FILE 'REGISTRY' ENTERED AT 12:49:44 ON 25 FEB 2003

L1 1 S POLYCARBOPHIL/CN

FILE 'CA' ENTERED AT 12:50:33 ON 25 FEB 2003

S 9003-97-8/REG#

FILE 'REGISTRY' ENTERED AT 12:50:59 ON 25 FEB 2003

L2 1 S 9003-97-8/RN

FILE 'CA' ENTERED AT 12:51:00 ON 25 FEB 2003

L3 303 S L2

L4 94527 S EYE OR OCULAR OR CORNEA#

L5 25 S L3 AND L4

FILE 'MEDLINE' ENTERED AT 12:59:00 ON 25 FEB 2003

L6 0 S 9003-97-8/RN

L7 71 S 9003-97-8

L8 198 S 130370-60-4

L9 0 S L7 AND L8

FILE 'CA' ENTERED AT 13:00:10 ON 25 FEB 2003

L10 169 S L8

L11 2 S L10 AND L3

=> log hold

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

9.40

52.58

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

TOTAL

ENTRY

SESSION

CA SUBSCRIBER PRICE

-1.24

-5.58

SESSION WILL BE HELD FOR 60 MINUTES

STN INTERNATIONAL SESSION SUSPENDED AT 13:03:14 ON 25 FEB 2003

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:sssptaul88sxs

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * Welcome to STN International * * * * *

NEWS 1 Web Page URLs for STN Seminar Schedule - N. America
NEWS 2 Apr 08 "Ask CAS" for self-help around the clock
NEWS 3 Apr 09 BEILSTEIN: Reload and Implementation of a New Subject Area
NEWS 4 Apr 09 ZDB will be removed from STN
NEWS 5 Apr 19 US Patent Applications available in IFICDB, IFIPAT, and IFIUDB
NEWS 6 Apr 22 Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS
NEWS 7 Apr 22 BIOSIS Gene Names now available in TOXCENTER
NEWS 8 Apr 22 Federal Research in Progress (FEDRIP) now available
NEWS 9 Jun 03 New e-mail delivery for search results now available
NEWS 10 Jun 10 MEDLINE Reload
NEWS 11 Jun 10 PCTFULL has been reloaded
NEWS 12 Jul 02 FOREGE no longer contains STANDARDS file segment
NEWS 13 Jul 22 USAN to be reloaded July 28, 2002;
saved answer sets no longer valid
NEWS 14 Jul 29 Enhanced polymer searching in REGISTRY
NEWS 15 Jul 30 NETFIRST to be removed from STN
NEWS 16 Aug 08 CANCERLIT reload
NEWS 17 Aug 08 PHARMAMarketLetter(PHARMAML) - new on STN
NEWS 18 Aug 08 NTIS has been reloaded and enhanced
NEWS 19 Aug 19 Aquatic Toxicity Information Retrieval (AQUIRE)
now available on STN
NEWS 20 Aug 19 IFIPAT, IFICDB, and IFIUDB have been reloaded
NEWS 21 Aug 19 The MEDLINE file segment of TOXCENTER has been reloaded
NEWS 22 Aug 26 Sequence searching in REGISTRY enhanced
NEWS 23 Sep 03 JAPIO has been reloaded and enhanced
NEWS 24 Sep 16 Experimental properties added to the REGISTRY file
NEWS 25 Sep 16 CA Section Thesaurus available in CAPLUS and CA
NEWS 26 Oct 01 CASREACT Enriched with Reactions from 1907 to 1985
NEWS 27 Oct 21 EVENTLINE has been reloaded
NEWS 28 Oct 24 BEILSTEIN adds new search fields
NEWS 29 Oct 24 Nutraceuticals International (NUTRACEUT) now available on STN
NEWS 30 Oct 25 MEDLINE SDI run of October 8, 2002
NEWS 31 Nov 18 DKILIT has been renamed APOLLIT
NEWS 32 Nov 25 More calculated properties added to REGISTRY
NEWS 33 Dec 02 TIBKAT will be removed from STN
NEWS 34 Dec 04 CSA files on STN
NEWS 35 Dec 17 PCTFULL now covers WP/PCT Applications from 1978 to date
NEWS 36 Dec 17 TOXCENTER enhanced with additional content
NEWS 37 Dec 17 Adis Clinical Trials Insight now available on STN
NEWS 38 Dec 30 ISMEC no longer available
NEWS 39 Jan 13 Indexing added to some pre-1967 records in CA/CAPLUS
NEWS 40 Jan 21 NUTRACEUT offering one free connect hour in February 2003
NEWS 41 Jan 21 PHARMAML offering one free connect hour in February 2003
NEWS 42 Jan 29 Simultaneous left and right truncation added to COMPENDEX,
ENERGY, INSPEC

NEWS EXPRESS January 6 CURRENT WINDOWS VERSION IS V6.01a,
CURRENT MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
AND CURRENT DISCOVER FILE IS DATED 01 OCTOBER 2002

NEWS HOURS STN Operating Hours Plus Help Desk Availability
 NEWS INTER General Internet Information
 NEWS LOGIN Welcome Banner and News Items
 NEWS PHONE Direct Dial and Telecommunication Network Access to STN
 NEWS WWW CAS World Wide Web Site (general information)

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* * * * * STN Columbus * * * * *

FILE 'HOME' ENTERED AT 14:39:37 ON 12 FEB 2003

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 14:40:16 ON 12 FEB 2003

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 11 FEB 2003 HIGHEST RN 488780-79-6

DICTIONARY FILE UPDATES: 11 FEB 2003 HIGHEST RN 488780-79-6

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

=> s batimastat/cn

L1 1 BATIMASTAT/CN

=> d

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS

RN 130370-60-4 REGISTRY

CN Butanediamide, N4-hydroxy-N1-[(1S)-2-(methylamino)-2-oxo-1-(phenylmethyl)ethyl]-2-(2-methylpropyl)-3-[(2-thienylthio)methyl]-, (2R,3S)-(9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

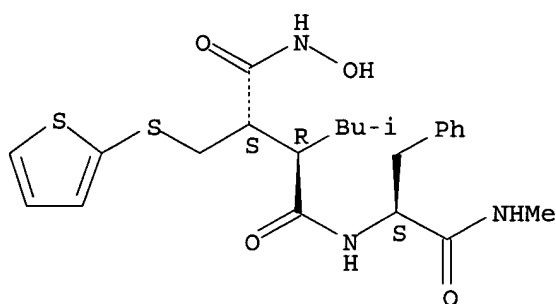
CN Butanediamide, N4-hydroxy-N1-[2-(methylamino)-2-oxo-1-(phenylmethyl)ethyl]-2-(2-methylpropyl)-3-[(2-thienylthio)methyl]-, [2R-[1(S*),2R*,3S*]]-

OTHER NAMES:

CN (2S,3R)-5-Methyl-3-[[(.alpha.S)-.alpha.-(methylcarbamoyl)phenethyl]carbamoyl]

• yl]-2-[(2-thienylthio)methyl]hexanohydroxamic acid
 CN Batimastat
 CN BB 94
 FS STEREOSEARCH
 MF C23 H31 N3 O4 S2
 CI COM
 SR CA
 LC STN Files: ADISINSIGHT, ADISNEWS, BIOBUSINESS, BIOSIS, BIOTECHNO, CA,
 CANCERLIT, CAPLUS, CBNB, CIN, DDFU, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES,
 EMBASE, IPA, MEDLINE, MRCK*, PHAR, PROMT, SYNTHLINE, TOXCENTER, USAN,
 USPATFULL
 (*File contains numerically searchable property data)
 Other Sources: WHO

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

167 REFERENCES IN FILE CA (1962 TO DATE)
 4 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
 169 REFERENCES IN FILE CAPLUS (1962 TO DATE)

=> file ca

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	6.30	6.51

FILE 'CA' ENTERED AT 14:40:59 ON 12 FEB 2003
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FILE COVERS 1907 - 6 Feb 2003 VOL 138 ISS 7
 FILE LAST UPDATED: 6 Feb 2003 (20030206/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l1
L2 167 L1

=> s 130370-60-4D
L3 4 130370-60-4D

=> s l2 or l3
L4 167 L2 OR L3

=> s eye or retina?
82181 EYE
17224 EYES
88075 EYE
(EYE OR EYES)
33063 RETINA?
L5 97565 EYE OR RETINA?

=> s l5 and l4
L6 9 L5 AND L4

=> d ti 1-9

L6 ANSWER 1 OF 9 CA COPYRIGHT 2003 ACS
TI Experimental studies of matrix metalloproteinase inhibitor on
retina neovascularization

L6 ANSWER 2 OF 9 CA COPYRIGHT 2003 ACS
TI Incensole and furanogermacrene and compounds in treatment for inhibiting
neoplastic lesions and microorganisms

L6 ANSWER 3 OF 9 CA COPYRIGHT 2003 ACS
TI Methods and compositions for treating and preventing posterior segment
ophthalmic disorders

L6 ANSWER 4 OF 9 CA COPYRIGHT 2003 ACS
TI Hapten-coagulation agent-antineoplastic agent combinations for treating
neoplasms

L6 ANSWER 5 OF 9 CA COPYRIGHT 2003 ACS
TI Methods of ophthalmic administration

L6 ANSWER 6 OF 9 CA COPYRIGHT 2003 ACS
TI Batimastat(British Biotech plc)

L6 ANSWER 7 OF 9 CA COPYRIGHT 2003 ACS
TI Use of neomycin for treating angiogenesis-related diseases

L6 ANSWER 8 OF 9 CA COPYRIGHT 2003 ACS
TI Medical use of matrix metalloproteinase (MMP) inhibitors for inhibiting
tissue contraction

L6 ANSWER 9 OF 9 CA COPYRIGHT 2003 ACS
TI Use of matrix metalloprotease (MMP) inhibitors as antitumor agents

=> d bib ab 1-9

L6 ANSWER 1 OF 9 CA COPYRIGHT 2003 ACS
AN 137:163594 CA
TI Experimental studies of matrix metalloproteinase inhibitor on
retina neovascularization
AU Nie, Xiaoyi; Chen, Shengju; Jin, Wanrong; Zhang, Wenfang
CS Department of Ophthalmology, the Second Hospital of Lanzhou Medical

College, Lanzhou, 730030, Peop. Rep. China
SO Yanke Yanjiu (2001), 19(6), 511-514
CODEN: YAYAFH; ISSN: 1003-0808

PB Henansheng Yanke Yanjiuso
DT Journal
LA Chinese

AB The therapeutic effects of the matrix metalloproteinases (MMP) inhibitor on the animal model of ischemic induced **retinal** neovascularization were studied. **Retina** neovascularization was induced in newborn mice exposed to 75% oxygen for five days, followed by room air. Then, the mice were subdivided into three groups, one group was used as control, the others received i.p. injections of a MMP inhibitor. Histol. anal. was done to quantitate the neovascular response in these animals. **Retinal** exts. underwent zymog. anal. to with induced **retina** neovascularization. **Retina** neovascularization was significantly inhibited with i.p. of a MMP inhibitor. A MMP inhibitor may have therapeutic potential in preventing **retina** neovascularization.

L6 ANSWER 2 OF 9 CA COPYRIGHT 2003 ACS

AN 137:88442 CA

TI Incensole and furanogermacrene and compounds in treatment for inhibiting neoplastic lesions and microorganisms

IN Shanahan-Pendergast, Elisabeth

PA Ire.

SO PCT Int. Appl., 68 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002053138	A2	20020711	WO 2002-IE1	20020102
	WO 2002053138	A3	20020919		
	W: AE, AG, AT, AU, BB, BG, CA, CH, CN, CO, CU, CZ, LU, LV, MA, MD, UA, UG, US, VN, YU, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, AT, BE, CH, CY, DE, ES, FI, ML, MR, NE, SN, TD, TG				

PRAI IE 2001-2 A 20010102

OS MARPAT 137:88442

AB The invention discloses the use of incensole and/or furanogermacrene, derivs. metabolites and precursors thereof in the treatment of neoplasia, particularly resistant neoplasia and immunodysregulatory disorders. These compds. can be administered alone or in combination with conventional chemotherapeutic, antiviral, antiparasite agents, radiation and/or surgery. Incensole and furanogermacrene and their mixt. showed antitumor activity against various human carcinomas and melanomas and antimicrobial activity against Staphylococcus aureus and Enterococcus faecalis.

L6 ANSWER 3 OF 9 CA COPYRIGHT 2003 ACS

AN 135:267265 CA

TI Methods and compositions for treating and preventing posterior segment ophthalmic disorders

IN Si, Erwin Chun-Chit; Bowman, Lyle M.; Rowe-Rendleman, Cheryl; Roy, Samir

PA Insite Vision Incorporated, USA

SO PCT Int. Appl., 52 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001068053	A2	20010920	WO 2001-US7171	20010307
	WO 2001068053	A3	20020829		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,				

CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU,
ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1261317 A2 20021204 EP 2001-914710 20010307

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRAI US 2000-523102 A 20000310 *mStart*
US 2000-648446 A 20000828
WO 2001-US7171 W 20010307

AB Methods and compns. for the prophylactic and therapeutic treatment of
ophthalmic disorders assocd. with the posterior segment of the **eye**
using topical ophthalmic compns. comprising therapeutic agents. The
invention specifically provides for methods and compns. for the
prophylactic and therapeutic treatment of **retinal** disorders
assocd. with neovascularization using topical ophthalmic compns.
comprising hydroxamic acid matrix metalloproteinase inhibitors such as
batimastat.

L6 ANSWER 4 OF 9 CA COPYRIGHT 2003 ACS
AN 135:117219 CA
TI Hapten-coagulation agent-antineoplastic agent combinations for treating
neoplasms
IN Yu, Baofa
PA USA
SO PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001052868	A1	20010726	WO 2001-US1737	20010118
	WO 2001052868	C2	20030116		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			

US 2002044919 A1 20020418 US 2001-765060 20010117

PRAI US 2000-177024P P 20000119

AB Methods are provided for treating neoplasms, tumors and cancers, using one
or more haptens and coagulation agents or treatments, alone or in
combination with other anti-neoplastic agents or treatments. Also
provided are combinations, and kits contg. the combinations for effecting
the therapy.

RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 5 OF 9 CA COPYRIGHT 2003 ACS
AN 132:156860 CA
TI Methods of ophthalmic administration
IN Bowman, Lyle M.; Pfeiffer, James F.; Clark, Leslie A.; Hecker, Karl I.
PA Insite Vision, Incorporated, USA
SO PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000007565	A2	20000217	WO 1999-US17543	19990802
	WO 2000007565	A3	20000511		
	W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
	CA 2339244	AA	20000217	CA 1999-2339244	19990802
	AU 9953327	A1	20000228	AU 1999-53327	19990802
	EP 1100462	A2	20010523	EP 1999-938953	19990802
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			
	JP 2002522373	T2	20020723	JP 2000-563251	19990802
	NO 2001000556	A	20010403	NO 2001-556	20010201
PRAI	US 1998-127920	A	19980803		
	WO 1999-US17543	W	19990802		

AB Intrascleral injection of a therapeutic or diagnostic material at a location overlying the retina provides a minimally invasive technique for delivering the agent to the posterior segment of the eye. The procedure also allows for close proximity of the material to the targeted site and can be effectively used to treat conditions assocd. with the posterior segment of the eye, including macular degeneration, vein occlusion, and diabetic retinopathy. The sclera can be used to hold a depot of the material such as for sustained released or as a conduit for propelling material through whereby the material is delivered immediately to the underlying tissues but without phys. penetrating the sclera with an instrument or otherwise unreasonably traumatizing the eye. A compn. for the PAF antagonist Lexipafant (BB-882) administration was prepd. contg. BB-882 1.0, HPMC 2.5, sorbitol 1.5, glycerol 1.0, Pluronic F-127 1.0, HCL (1N) 5.0, NaOH (2N) q.s. to pH 7.4, and water q.s. to 100% wt./wt.

L6 ANSWER 6 OF 9 CA COPYRIGHT 2003 ACS
AN 132:146059 CA
TI Batimastat (British Biotech plc)
AU Jiang, Wen G.
CS Metastasis Research Group, University of Wales College of Medicine, Cardiff, CF14 4XN, UK
SO Current Opinion in Oncologic, Endocrine & Metabolic Investigational Drugs (1999), 1(5), 525-535
CODEN: COODF2; ISSN: 1464-8466

PB Current Drugs Ltd.
DT Journal; General Review
LA English

AB A review with .apprx.170 refs. InSite Vision is developing the non-specific metalloproteinase inhibitor, batimastat, licensed from British Biotech for ophthalmic indications, for the potential treatment of pterygia, for which phase II trials have commenced [260337], [267891]. Batimastat is also in preclin. studies for the treatment of atherosclerosis. Results showed that MMP inhibition by the drug resulted in 50% redn. of lumen loss following angioplasty in the Yucatan micropig [315357]. British Biotech discontinued development of batimastat for cancer indications because it had a similar compd., marimastat (qv), in development with a more favorable administration profile [226981], [227801]. InSite is developing batimastat with its proprietary DuraSite * eyedrop system. In August 1997, a phase II study commenced to evaluate batimastat's safety and preliminary efficacy during a three-month course

not topical

order 1

of treatment following surgical removal of pterygia. Up to 20 patients, who will be followed for one year following surgery, will be enrolled in the double-masked, placebo-controlled trial [260337]. The first reported phase II trial for pterygia commenced in Dec. 1994 [279819], [170300], [177060]. This was a randomized, placebo-controlled, double-masked trial. A total of 40 patients, who had undergone surgery for removal of a primary pterygium, were to receive either a 0.1% dose of batimastat 0.3% dose or a vehicle three times daily for 30 days [180494]. Earlier phase II trials for malignant ascites were halted by British Biotech following an unexpectedly high incidence of side-effects, which were attributed to changes in the manufg. process during scale-up for larger trials. Regulatory approval was received in June 1995 for the restart of these trials, and the company reverted to the earlier prodn. method [173287], [174190], [184484]. Batimastat showed encouraging results in a phase I/II study of 15 patients with malignant ascites and a further phase II trial was completed involving 40 patients with malignant ascites. Batimastat was the first matrix metalloproteinase inhibitor to enter clin. trials for the treatment of cancer [181776]. Batimastat is claimed in British Biotech's patent application WO-09005719.

RE.CNT 176 THERE ARE 176 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 7 OF 9 CA COPYRIGHT 2003 ACS
AN 131:346535 CA
TI Use of neomycin for treating angiogenesis-related diseases
IN Hu, Guo-Fu; Vallee, Bert L.
PA The Endowment for Research In Human Biology, Inc., USA
SO PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9958126	A1	19991118	WO 1999-US10269	19990511
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2331620	AA	19991118	CA 1999-2331620	19990511
AU 9939804	A1	19991129	AU 1999-39804	19990511
EP 1083896	A1	20010321	EP 1999-922915	19990511
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 6482802	B1	20021119	US 2000-700436	20001109
PRAI US 1998-84921P	P	19980511		
WO 1999-US10269	W	19990511		

AB The present invention is directed to using neomycin or an analog thereof as a therapeutic agent to treat angiogenesis-related diseases, which are characterized by excessive, undesired or inappropriate angiogenesis or proliferation of endothelial cells. The present invention is also directed to pharmaceutical compns. comprising: (a) neomycin or an analog and, optionally, (b) another anti-angiogenic agent or an anti-neoplastic agent. The present invention is further directed to a method for screening neomycin analogs having anti-angiogenic activity. A preferred embodiment of the invention relates to using neomycin to treat subjects having such diseases. A dose of 20 ng neomycin/embryo or higher completely inhibited angiogenin-induced angiogenesis in the chorioallantoic membrane (CAM) assay. Neomycin inhibits angiogenin-induced angiogenesis mainly through inhibition of nuclear

translocation of angiogenin.

RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 8 OF 9 CA COPYRIGHT 2003 ACS
AN 123:330041 CA
TI Medical use of matrix metalloproteinase (MMP) inhibitors for inhibiting
tissue contraction
IN Khaw, Peng Tee; Schultz, Gregory Scott
PA Institute of Ophthalmology, UK; University of Florida
SO PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9524921	A1	19950921	WO 1995-GB576	19950316
	W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, DK, EE, ES, FI, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SG				
	RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9518985	A1	19951003	AU 1995-18985	19950316
	EP 750512	A1	19970102	EP 1995-911409	19950316
	R: CH, DE, FR, GB, IT, NL				
	US 6093398	A	20000725	US 1996-716155	19961119
	US 6379667	B1	20020430	US 1999-368307	19990803
	US 2002164319	A1	20021107	US 2002-135934	20020429
PRAI	GB 1994-5076	A	19940316		
	WO 1995-GB576	W	19950316		
	US 1996-716155	A3	19961119		
	US 1999-368307	A3	19990803		
AB	An MMP inhibitor, esp. a collagenase inhibitor, is useful in the manuf. of a medicament for the treatment of a natural or artificial tissue contg. extracellular matrix components to inhibit contraction of the tissue, e.g. to prevent scar contracture in the skin or eye, by inhibiting invasion of the tissue by fibroblasts. This effect was demonstrated in collagen gels seeded with ocular fibroblasts and treated with the MMP inhibitor Galardin or with antibodies to MMP 1, 2, or 3.				

L6 ANSWER 9 OF 9 CA COPYRIGHT 2003 ACS
AN 120:95761 CA
TI Use of matrix metalloprotease (MMP) inhibitors as antitumor agents
IN Brown, Peter Duncan; Bawden, Lindsay Jayne; Miller, Karen Margrete
PA British Bio-Technology Ltd., UK
SO PCT Int. Appl., 48 pp.
CODEN: PIXXD2

DT Patent
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9321942	A2	19931111	WO 1993-GB888	19930429
	WO 9321942	A3	19940120		
	W: AU, BR, CA, CZ, FI, HU, JP, KR, NO, NZ, PL, PT, RU, SK, UA, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9342672	A1	19931129	AU 1993-42672	19930429
	EP 1002556	A2	20000524	EP 1999-114903	19930429
	EP 1002556	A3	20010110		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
	ZA 9303089	A	19931123	ZA 1993-3089	19930430

41 US 5872152 A 19990216 US 1996-686485 19960726
 PRAI GB 1992-9513 A 19920501
 GB 1993-5817 A 19930320
 EP 1993-911883 A3 19930429
 WO 1993-GB888 A 19930429
 US 1993-133081 B1 19931202

OS MARPAT 120:95761

AB Various known hydroxamic acid MMPs are useful in the prepn. of agents for
 promoting tumor regression and/or inhibiting cancer cell proliferation.
 Thus, I inhibited proliferation of human melanoma cells in vitro at 3
 .mu.M, and markedly increased the survival time of mice bearing a human
 ovarian carcinoma xenograft when administered at 40 mg/kg/day i.p.

=> file wpids

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	30.63	37.14

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-5.58	-5.58

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 MOST RECENT DERWENT UPDATE: 200310 <200310/DW>
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 GUIDES, PLEASE VISIT:
http://www.derwent.com/userguides/dwpi_guide.html <<<

=> s batimastat

L7 13 BATIMASTAT

=> s (metalloproteinase or metalloprotease) (w) inhibitor

737 METALLOPROTEINASE
 242 METALLOPROTEINASES
 855 METALLOPROTEINASE
 (METALLOPROTEINASE OR METALLOPROTEINASES)
 490 METALLOPROTEASE
 142 METALLOPROTEASES
 570 METALLOPROTEASE
 (METALLOPROTEASE OR METALLOPROTEASES)
 47774 INHIBITOR
 36137 INHIBITORS

74218 INHIBITOR

(INHIBITOR OR INHIBITORS)

L8 477 (METALLOPROTEINASE OR METALLOPROTEASE) (W) INHIBITOR

=> s eye or retinal or retina

44180 EYE

15128 EYES

52439 EYE

(EYE OR EYES)

2307 RETINAL

1 RETINALS

2307 RETINAL

(RETINAL OR RETINALS)

2578 RETINA

63 RETINAS

61 RETINAE

2638 RETINA

(RETINA OR RETINAS OR RETINAE)

L9 54609 EYE OR RETINAL OR RETINA

=> s (l7 or l8) and l9

L10 24 (L7 OR L8) AND L9

=> d bib ab 1-24

L10 ANSWER 1 OF 24 WPIDS (C) 2003 THOMSON DERWENT

AN 2002-625807 [67] WPIDS

CR 2000-195436 [17]

DNN N2002-494805 DNC C2002-176407

TI New method for intrasccleral injection of a therapeutic/diagnostic agent useful for e.g. treating cystoid macular edema, age-related macular degeneration, diabetic retinopathy, **retinal** artery or vein occlusion and retinopathy.

DC B07 P31

IN BOWMAN, L M; CLARK, L A; HECKER, K I; PFEIFFER, J F

PA (INSI-N) INSITE VISION INC

CYC 1

PI US 6397849 B1 20020604 (200267)* 12p

ADT US 6397849 B1 CIP of US 1998-127920 19980803, US 1999-366072 19990802

PRAI US 1999-366072 19990802; US 1998-127920 19980803

AB US 6397849 B UPAB: 20021018

NOVELTY - New method for an intrasccleral injection comprises injecting therapeutic or diagnostic material into the scleral layer over the posterior segment of the **eye** through a location on the exterior surface of the sclera that overlies **retinal** tissue with a cannula along an axis of insertion.

The cannula has an aperture located on the side and is orientated toward the interior surface of the sclera.

ACTIVITY - Ophthalmological; Antidiabetic.

MECHANISM OF ACTION - None given in the source material.

USE - The method is useful for treating ocular disease, especially cystoid macular edema, age-related macular degeneration, diabetic retinopathy, diabetic maculopathy, central **retinal** artery occlusion, central **retinal** vein occlusion, branch **retinal** artery occlusion, branch **retinal** vein occlusion, retinopathy of prematurity, sickle cell retinopathy, photic retinopathy, radiation retinopathy, **retinal** detachment, retinitis pigmentosa, macular hole, cataract and glaucoma (all claimed).

ADVANTAGE - The method provides a minimally invasive technique for delivering an agent to the posterior segment of the **eye**.
Dwg.0/1

L10 ANSWER 2 OF 24 WPIDS (C) 2003 THOMSON DERWENT

AN 2002-547434 [58] WPIDS

DNC C2002-155166

not topical

* TI New spiro-pyrimidine-2,4,6-trione derivatives, useful in treatment of various disorders e.g. cancer, are metalloendopeptidase and matrix metalloproteinase inhibitors.

DC B02

IN BRONK, B S; NOE, M C; WYTHES, M J

PA (PFIZ) PFIZER PROD INC

CYC 97

PI WO 2002034753 A2 20020502 (200258)* EN 75p

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ

NL OA PT SD SE SL SZ TR TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK

DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR

KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO

RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2002010813 A 20020506 (200258)

ADT WO 2002034753 A2 WO 2001-IB1986 20011023; AU 2002010813 A AU 2002-10813 20011023

FDT AU 2002010813 A Based on WO 200234753

PRAI WO 2000-243389P 20001026

AB WO 200234753 A UPAB: 20020910

NOVELTY - Spiro-pyrimidine-2,4,6-trione Compounds are new.

DETAILED DESCRIPTION - Spiro-pyrimidine-2,4,6-trione compound of formula (I) is new.

A = group of formula (Ia) - (Ig);

A' = C(O) or SO₂;

B' = C(R₁₀)(R₁₁), SO₂ or C(O);

C' = C(R₅)(R₆) or R₁₂;

D' = C(R₁)(R₂) or C(O);

E' = C(O), SO₂ or C(R₁₁)(R₁₀);

F' = C(R₄)(R₃) or C(R₈)(R₇);

G' = C(O), SO₂ or C(R₁₁)(R₁₀);

H' = C(R₈)(R₇) or C(R₁₃)(R₁₂);

R₁ - R₁₃ = 1-4C alkyl, 6-10C aryl, 1-10C heteroaryl, 3-8C cycloalkyl, 1-10C heterocyclyl (all optionally substituted on any ring carbon atom capable of forming an addition bond with mono- or tri-substituents per ring selected from halo, 1-4C alkyl, 1-4C alkoxy, CN, OH or NH₂), H, 1-4C alkenyl or 1-4C alkynyl;

X = 6-10C aryl or 1-10C heteroaryl (all optionally substituted on any of the ring carbon atoms capable of forming an additional bond by mono- or di-substituents per ring selected from T);

T = F, Cl, Br, CN, OH, 1-4C alkyl, 1-4C perfluoroalkyl, 1-4C perfluoroalkoxy, 1-4C alkoxy or 3-8C cycloalkoxy);

Y = a bond, O, S, -C=O, -SO₂, S=O, CH₂, CH₂O, O(CH₂)_n, CH₂S, S(CH₂)_n, CH₂SO, CH₂SO₂, SO(CH₂)_n, SO₂(CH₂)_n, NR₁₄, NR₁₄(CH₂)_n, CH₂(N(R₁₄)), CH₂(CH₂)_n, CH=CH, C equivalent to C, (N(R₁₄))-SO₂ or SO₂(N(R₁₄));

n = 1 - 4;

R₁₄ = H or 1-4C alkyl;

Z = 3-8C cycloalkyl, 1-10C heterocyclyl, 6-10C aryl or 1-10C heteroaryl (all optionally substituted on any of the ring carbon atoms capable of forming an additional bond by mono- or di-substituents per ring selected from T) where one or two carbon-carbon single bonds of 3-8C cycloalkyl, 1-10C heterocyclyl may optionally be replaced by carbon-carbon double bond;

G = R₁₅-(CR₁₆R₁₇)_p where G is a substituent on any ring carbon atom of Z capable of forming an additional bond and is oriented at a position other than alpha to the point of attachment of the Z ring to Y;

p = 0 - 4;

R₁₅ = halo, -CN, NO₂, OH, 1-4C alkenyl, 1-4C alkynyl, 1-4C perfluoroalkyl, perfluoro(1-4C)alkoxy, R₁₈, R₁₈-O, R₁₈-(1-4C alkyl)-O, R₁₈-C(=O), R₁₈-(C=O)-O, R₁₈-O(C=O), R₁₈-S, R₂₂-(S=O), R₁₈-(SO₂)-, R₂₂-(SO₂)(NR₂₁), R₁₉-(C=O)(NR₂₁), R₂₂-O(C=O)(NR₂₁), (R₁₉R₂₀)N-, (R₁₉R₂₀)N(SO₂), (R₁₉R₂₀)N-(C=O), (R₁₉R₂₀)N-(C=O)(NR₂₁) or (R₁₉R₂₀)N-(C=O)O;

R₁₆ and R₁₇ = H or 1-4C alkyl;

NPA

R16 + R17 = 5 - 10-membered carbocyclic ring;
R18 - R21 = 3-8C cycloalkyl, 1-10C heterocyclyl (both optionally substituted by oxo), 6-10C aryl, 1-10C heteroaryl (all optionally substituted on any of the ring carbon atoms capable of forming an additional bond by mono- - tri-substituents per ring selected from T, NH₂, 1-4C alkyl-NH-, or (1-4C alkyl)₂-N and further 1-10C heteroaryl and 1-10C heterocyclyl may optionally be substituted on any ring nitrogen atom to support an additional substituent by one or two substituents per ring selected from 1-4C alkyl or 1-4C alkyl-(C=O)) H or 1-4C alkyl;

N(R19 + R20) and N(R19 + R21) = 3 - 8-membered heterocyclic ring;
R22 = 1-10C heterocyclyl, 3-8C cycloalkyl (both optionally substituted by oxo), 1-10C heteroaryl or 6-10C aryl (all optionally substituted on any of the ring carbon atoms capable of forming an additional bond by mono- - tri-substituents per ring selected from T, NH₂, 1-4C alkyl-NH-, or (1-4C alkyl)₂-N and further 1-10C heteroaryl and 1-10C heterocyclyl may optionally be substituted on any ring nitrogen atom to support an additional substituent by one or two substituents per ring selected from 1-4C alkyl or 1-4C alkyl-(C=O)) or 1-4C alkyl;

N(R21 + R22), O(R21+R22) or S(R21+R22) = 3 - 8 heterocyclic ring.
Provided that when C' is C(R6)(R5) then D' is C(R1)(R2); When C' is R12 then D' is C(O); When F' is C(R4)(R3) then E' is C(O) or S(O)₂; When E' is C(R11)(R10) then F' is C(R8)(R7); When H' is C(R4)(R3) then G' is C(O) or SO₂; and When H' is C(R13)(R12) then G' is C(R11)(R10).

INDEPENDENT CLAIMS are also included for:

(1) A pharmaceutical composition for treating a condition of a mammal by the inhibition of matrix metalloproteins; and

(2) A method for treating various diseases claimed.

ACTIVITY - Tranquilizer; Osteopathic; Antiarthritic; Cytostatic; Antirheumatic; Antigout; Gastrointestinal-Gen; Antipsoriatic; Antifungal; Hepatotropic; Antiinflammatory; Antiulcer; Immunomodulator; Antiasthmatic; Antibacterial; Virucide; Anti-HIV; Antipyretic; Protozoacide; Immunosuppressive; Hemostatic; Antiarteriosclerotic; Cardiant; Cerebroprotective; Vasotropic; ~~Ophthalmological~~; Antidiabetic; Neuroprotective; Nootropic; Anticonvulsant; Antiparkinsonian; Antitumor; Antimigraine; Antidepressant; Nephrotropic; Gynecological; Analgesic; Antipsoriatic; Dermatological; Vulnerary; Antiallergic.

MECHANISM OF ACTION - Metalloendopeptidases inhibitor; Matrix metalloproteinases inhibitor.

Test details are described but no results are given.

USE - (I) are used in the treatment of conditions of connective tissue disorders, inflammatory disorder, immunology/allergy disorder, infectious diseases, respiratory diseases, cardiovascular disease, eye diseases, metabolic diseases, central nervous system disorder, liver/kidney disease, reproductive health disorder, gastric disorder, skin disorder and cancer in a mammal (e.g. human) (claimed). Connective tissue disorders e.g. traumatic joint injury, osteoporosis, Paget's disease, loosening of artificial joint implants, periodontal disease and gingivitis. Destruction of articular cartilage e.g. connective tissue disorders resulting in articular cartilage destruction, arthritis, Inflammatory disorders e.g. ankylosing spondylitis, chondrocalcinosis and gout. Immunology/allergy disorders e.g. organ transplant toxicity, granulomatous inflammation/tissue remodeling immunosuppression and sarcoid. Infectious diseases e.g. malaria, sepsis, hemodynamic shock and septic shock. Respiratory diseases e.g. chronic obstructive pulmonary disease hyperoxic alveolar injury and idiopathic pulmonary fibrosis and other fibrotic lung diseases. Cardiovascular diseases e.g. atherosclerosis and brain aortic aneurysm, congestive heart failure, stroke, cerebral ischemia, coagulation and acute phase response, left ventricular dilation, post ischemic reperfusion injury, hemangiomas, restenosis and eye diseases. Metabolic diseases e.g. diabetes. Central Nervous System (CNS) disorders e.g. head trauma, Alzheimer's disease, demyelinating diseases of the nervous system, Huntington's disease and multiple sclerosis. Liver/Kidney diseases e.g. cirrhosis of the liver and interstitial nephritis. Reproductive health disorders e.g. endometriosis, contraception and abortifacient. Gastric disorders e.g. colonic anastomosis and gastric

ulcers. Skin disorders e.g. skin aging, pressure sores and scleritis.
Dwg.0/0

L10 ANSWER 3 OF 24 WPIDS (C) 2003 THOMSON DERWENT

AN 2002-547431 [58] WPIDS

DNC C2002-155163

TI New pyrimidine-2,4,6-trione **metalloproteinase inhibitors**
useful for treating conditions such as inflammation, or cancer.

DC B03

IN NOE, M C; REITER, L A; WYTHES, M J

PA (PFIZ) PFIZER PROD INC; (NOEM-I) NOE M C; (REIT-I) REITER L A; (WYTH-I)
WYTHES M J

CYC 97

PI WO ~~2002034726~~ A2 20020502 (200258)* EN 70p

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
NL OA PT SD SE SL SZ TR TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO
RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2002010800 A 20020506 (200258)

US 2002132822 A1 20020919 (200264)

ADT WO 2002034726 A2 WO 2001-IB1953 20011017; AU 2002010800 A AU 2002-10800
20011017; US 2002132822 A1 Provisional US 2000-243314P 20001026, US
2001-32837 20011025

FDT AU 2002010800 A Based on WO 200234726

PRAI US 2000-243314P 2000/10/26; US 2001-32837 20011025

AB WO 200234726 A UPAB: 20021031

NOVELTY - Pyrimidine-2,4,6-trione compounds or their salts are new.

DETAILED DESCRIPTION - Pyrimidine-2,4,6-trione compounds of formula
(I) or their salts are new.

A = 6-10C aryl or 1-10C heteroaryl (both optionally substituted);

B = aryl or alkyl;

X = O, -C=O, -S, -SO₂, S=O or CH₂O;

Y = e.g. O, -C=O, -S, -SO₂, -S=O, NR₁₀ or CH₂O;

R₁ = e.g. H, (R₂)_{2n+1}-(C)_n- or optionally substituted alkyl.

Full definitions are given in the DEFINITIONS (full definitions and
preferred definitions) section.

ACTIVITY - Antiinflammatory; Antiallergic; Virucide; Cardiant;
Ophthalmological; Dermatological; Cytostatic; Antipsoriatic;
Antirheumatic; Osteopathic; Antiarthritic; Antiulcer; Antigout;
Immunomodulator; Vulnerary; Nootropic; Immunosuppressive; Antiasthmatic;
Antiartherosclerotic; Antibacterial; Protozoacide; Anti-HIV; Hepatotropic;
Antimigraine; Vasotropic; Tranquillizer; Antidiabetic; Neuroprotective;
Anticonvulsant; Antiparkinsonian; Analgesic; Cerebroprotective;
Antidepressant; Gynecological.

MECHANISM OF ACTION - Pyrimidine-2,4,6-trione
metalloproteinase inhibitor; Zinc metalloendopeptidases
inhibitor; Matrix metalloproteinases (MMP) (e.g. MMP-1 - MMP-20)
inhibitor.

Test details are described no results are given.

USE - These novel compounds are used in a composition for treating
connective tissue disorders, inflammatory disorders, immunology/allergy
disorders, infectious diseases, respiratory diseases, cardiovascular
diseases, **eye** disease, metabolic diseases, central nervous
system (CNS) disorders, liver/kidney diseases, reproductive health
disorders, gastric disorders, skin disorders or cancers in a mammal (e.g.
human) (claimed) e.g. degenerative cartilage loss following traumatic
joint injury, osteoarthritis, osteoporosis, Paget's disease, loosening of
artificial joint implants, periodontal disease, gingivitis, juvenile
rheumatoid arthritis, ankylosing spondylitis, psoriasis,
chondrocalcinosis, gout, inflammatory bowel disease, ulcerative colitis,
Crohn's disease, cachexia, organ transplant toxicity, allergic reactions,
allergic contact hypersensitivity, autoimmune disorders, asthma, septic
arthritis, AIDS, fever, prion diseases, myasthenia gravis, malaria,

sepsis, hemodynamic shock, septic shock, chronic obstructive pulmonary disease, emphysema, atherosclerosis, congestive heart failure, myocardial and cerebral infarction, stroke, cerebral ischemia, coagulation, acute phase response, left ventricular dilation, post ischemic reperfusion injury, angiofibromas, hemangiomas, restinosis, ocular angiogenesis, keratoconus, sjogren's syndrome, myopia, ocular tumor, corneal graft rejection, neovascular glaucoma, retinopathy of prematurity, diabetes, head trauma, Alzheimer's disease, demyelinating diseases of nervous system, Huntington's disease, Parkinson's disease, peripheral neuropathy, pain, cerebral amyloid angiopathy, nootropic or cognition enhancement, amyotrophic lateral sclerosis, multiple sclerosis, migraine, depression, anorexia, glomerulonephritis, endometriosis, contraception (male/female), dysmenorrhea, colon, anastomosis, gastric ulcers, skin aging, eczema, dermatitis, epidermalysis, bullosa, abnormal wound healing, burns scleritis, colon cancer, breast cancer.

ADVANTAGE - (I) selectively inhibits MMP-13 preferentially over MMP-1 or MMP-13 over MMP-1 and MMP-14 or MMP-1 and MMP-12.
Dwg.0/6

L10 ANSWER 4 OF 24 WPIDS (C) 2003 THOMSON DERWENT
AN 2002-540562 [58] WPIDS
DNC C2002-153294
TI Use of phanquinone, clioquinol, or their mixtures for the prevention and treatment of age-related macular or vitreo-**retinal** degeneration.
DC B05
IN XILINAS, M
PA (XILI-I) XILINAS M
CYC 99
PI FR 2819187 A1 20020712 (200258)* 33p
WO 2002055081 A2 20020718 (200258) EN
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
NL OA PT SD SE SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT
RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
ADT FR 2819187 A1 FR 2000-16369 20010110; WO 2002055081 A2 WO 2001-IB2265
20011128
PRAI FR 2000-16369 20010110
AB FR 2819187 A UPAB: 20020910
NOVELTY - The use of phanquinone (4,7-phenanthroline-5,6-dione) or clioquinol (5-chloro-7-iodo-8-quinolinol) or their mixtures (I) in compositions for the prevention and treatment of age-related macular degeneration (ARMD) due to extracellular matrix metalloproteinases (MMPs), is new.
ACTIVITY - Ophthalmological.
MECHANISM OF ACTION - (I) are **metalloproteinase inhibitors** by chelating with zinc.
USE - Prevention and treatment of age-related macular or vitreo-**retinal** degeneration.
Dwg.0/0

L10 ANSWER 5 OF 24 WPIDS (C) 2003 THOMSON DERWENT
AN 2002-527397 [56] WPIDS
DNC C2002-149311
TI New mesylate or chloride salt of tyrosine kinase inhibitor compounds useful for treating or preventing e.g. cancer.
DC B02
IN FRALEY, M E; KARKI, S B; KIM, Y
PA (MERI) MERCK & CO INC; (FRAL-I) FRALEY M E; (KARK-I) KARKI S B; (KIMY-I) KIM Y
CYC 96
PI WO 2002032861 A2 20020425 (200256)* EN 73p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
NL OA PT SD SE SL SZ TR TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KR KZ
LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU
SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2002026877 A 20020429 (200256)

US 2002072526 A1 20020613 (200256)

ADT WO 2002032861 A2 WO 2001-US32508 20011017; AU 2002026877 A AU 2002-26877
20011017; US 2002072526 A1 Provisional US 2000-241043P 20001017, US
2001-981979 20011017

FDT AU 2002026877 A Based on WO 200232861

PRAI US 2000-241043P 20001017; US 2001-981979 20011017

AB WO 200232861 A UPAB: 20020903

NOVELTY - Mesylate or chloride salt of 3-(5-(4-methanesulfonyl-piperazin-1-ylmethyl)-1H-indol-2-yl)-1H-quinolin-2-one, 3-(5-(4-methyl-5-oxo-(1,4)diazepan-1-ylmethyl)-1H-indol-2-yl)-1H-quinolin-2-one, 3-(5-(4-(2-hydroxy-ethanoyl)-piperazin-1-ylmethyl)-1H-indol-2-yl)-1H-quinolin-2-one and 3-(5-(2-((2-methoxyethyl)(methyl)amino)ethoxy)-1H-indol-2-yl)quinolin-2(1H)-one are new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:
(1) treating or preventing cancer involving administering the salt and paclitaxel, trastuzumab or GPIIb/IIIa antagonist (e.g. tirofiban) and
(2) compositions comprising one of the new salts and a carrier.

ACTIVITY - Cytostatic; Antidiabetic; Ophthalmological;
Antiinflammatory; Antirheumatic; Antiarthritic; Antipsoriatic;
Dermatological; Osteopathic; Cerebroprotective.

MECHANISM OF ACTION - Tyrosine kinase inhibitor, regulator and/or modulator.

Test details are described but no results are given.

USE - For treating or preventing cancer (e.g. cancer of brain, genitourinary tract, lymphatic system, stomach larynx, lung histiocyte lymphoma, lung adenocarcinoma, small cell lung cancer, pancreatic cancer, glioplastomas and breast carcinoma); angiogenesis, ocular disease, retinal vascularization, diabetic retinopathy, age related macular degeneration, inflammatory disease (e.g. rheumatoid arthritis, psoriasis, contact dermatitis and delayed hypersensitivity reactions); tyrosine kinase-dependent disease or condition, bone associated pathologies (e.g. osteosarcoma, osteoarthritis and rickets) and damage following a cerebral ischemic event (all claimed).

ADVANTAGE - The salts enhances pharmaco-kinetic properties as compared to compounds previously reported.
Dwg.0/3

L10 ANSWER 6 OF 24 WPIDS (C) 2003 THOMSON DERWENT

AN 2002-415731 [44] WPIDS

CR 2002-383050 [41]; 2002-404697 [43]; 2002-489672 [52]; 2002-599247 [64]

DNC C2002-117327

TI Targeting peptides identified by phage display, useful for targeting delivery to an organ or tissue, particularly for treating a disease, e.g. cancer, inflammatory or autoimmune diseases, infections or cardiovascular disease.

DC B04 D16

IN ARAP, W; PASQUALINI, R

PA (TEXA) UNIV TEXAS SYSTEM

CYC 97

PI WO 2002020769 A1 20020314 (200244)* EN 317p

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
NL OA PT SD SE SL SZ TR TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO
RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2001088843 A 20020322 (200251)

ADT WO 2002020769 A1 WO 2001-US27692 20010907; AU 2001088843 A AU 2001-88843
20010907

FDT AU 2001088843 A Based on WO 200220769

"PRAI US 2001-765101 20010117; US 2000-231266P 20000908

AB WO 200220769 A UPAB: 20021010

NOVELTY - An isolated peptide of 100 amino acids or less in size, is new. The peptide comprises at least 3 contiguous amino acids of a sequence selected from any of 243 sequences fully defined in the specification.

DETAILED DESCRIPTION - An isolated peptide of 100 amino acids or less in size. The peptide comprises at least 3 contiguous amino acids of a sequence selected from any of 243 sequences fully defined in the specification. The sequences are designated P5-P45, P47-P121, P123 or P-125-P250, e.g.:

P7: CTGGCVVDCLSLIC;
P8: CGVPCRPAACRGLC;
P9: CAGFCVPGCHSKC;
P10: CAGACPVGCGTGC;
P11: AERLWRS;
P47: TREVHRS;
P48: TRNTGNI;
P49: FDGQDRS;
P50: WGPKRL;
P51: WGESRL;
P123: CPRECESIC;
P125: CYNLCIRECESICGADGACWTWCADGCSRSC;
P126: CLGQCASICVNDC;
P127: CPKVCPRECESNC;
P128: CGTGCAVECEVVC;
P179: ALR; or
P180: CEALRLRAC.

INDEPENDENT CLAIMS are also included for the following:

- (1) a method (I) comprising:
 - (a) injecting a subject with a phage display library;
 - (b) obtaining samples of one or more organs or tissues;
 - (c) producing thin sections of the samples; and
 - (d) recovering phage from the thin sections;
- (2) a method (II) of preparing a phage display library;
- (3) a phage display library (III) prepared by the method;
- (4) a method (IV) of interfering with pregnancy by obtaining a peptide comprising at least 3 contiguous amino acids of any of P39-P45 and administering the peptide to the female;
- (5) a method (V) of delivering an agent to a fetus by obtaining a peptide comprising at least 3 contiguous amino acids of any of P39-P45, attaching the peptide to an agent, and administering the peptide to a pregnant subject;
- (6) method (VI) of targeting delivery to, adipose tissue, an organ or tissue, prostate cancer or angiogenic tissue;
- (7) a composition (VII) comprising the isolated peptide;
- (8) an antibody (VIII) that selectively binds to the isolated peptide;
- (9) a method (IX) comprising:
 - (a) injecting a subject with a phage display library;
 - (b) recovering at least one sample of at least one organ, tissue or cell type;
 - (c) separating the sample into isolated cells or clumps of cells;
 - (d) centrifuging the cells through an organic phase to form a pellet; and recovering the phage from the pellet;
- (10) a gene therapy vector (X) that expresses a targeting peptide sequence as part of a surface protein, where the targeting peptide comprises the isolated peptide cited above;
- (11) a method (XI) of diagnosing prostate cancer;
- (12) a method (XII) of identifying targeting peptides to angiogenic tissue;
- (13) methods (XIII) of inducing apoptosis in a cell;
- (14) a method (XIV) of modulating angiogenesis by obtaining a peptide comprising at 3 contiguous amino acids comprising any of P93-P131, and administering the peptide to the subject;
- (15) a method (XV) for detecting receptors for endostatin or

angiostatin; and

(16) a kit (XVI) comprising the isolated peptide and a control peptide, each in a container.

ACTIVITY - Cytostatic; antiinflammatory; antidiabetic; cardiovascular; immunomodulator; antibacterial; antiviral.

No biological data given.

MECHANISM OF ACTION - Gene therapy.

USE - The peptide is useful for targeting delivery to an organ or tissue, particularly for treating a disease, e.g. cancer, arthritis, diabetes, inflammatory disease, atherosclerosis, autoimmune disease, bacterial infection, viral infection, cardiovascular disease or degenerative disease. The peptide is also useful for inducing apoptosis in a subject, particularly to a subject with ischemia, cancer, arthritis, diabetes, cardiovascular disease, inflammation or macular degeneration (all claimed). Furthermore, the peptide is useful for diagnosing the diseases cited above.

Dwg.0/31

L10 ANSWER 7 OF 24 WPIDS (C) 2003 THOMSON DERWENT

AN 2002-393846 [42] WPIDS

DNN N2002-308808 DNC C2002-110763

TI New isolated human or mouse targeting peptide useful for targeted delivery of therapeutic agents, for inhibiting angiogenesis, tumor growth or pregnancy, and for inducing apoptosis or weight loss.

DC B04 D16 S03

IN KAUL, S C; SUGIHARA, T; WADHWA, R

PA (CHUG-N) CHUGAI RES INST MOLECULAR MEDICINE INC; (NAAD-N) NAT INST ADVANCED IND SCI & TECHNOLOGY

CYC 96

PI WO 2002020770 A1 20020314 (200242)* JA 317p

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
NL OA PT SD SE SL SZ TR TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KR KZ
LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU
SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2001084454 A 20020322 (200251)

ADT WO 2002020770 A1 WO 2001-JP7732 20010906; AU 2001084454 A AU 2001-84454 20010906

FDT AU 2001084454 A Based on WO 200220770

PRAI JP 2000-274209 20000908

AB WO 200220770 A UPAB: 20020704

NOVELTY - An isolated human or mouse targeting peptide (I) of 100 amino acids or less in size, comprising at least 3 contiguous amino acids of a fully defined sequence (S) selected from 243 sequences as given in the specification, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a method (M1) involving injecting a subject with a phage display library, obtaining samples of one or more organs or tissues, producing thin sections of samples, and recovering phage from the thin sections;

(2) preparing (M2) a phage display library, by immunizing a host animal with a target organ, tissue or cell type, obtaining mRNAs encoding antibodies from the host animal, preparing cDNAs from the mRNAs encoding antibodies, and preparing a phage display library from the cDNAs;

(3) a phage display library (II) prepared by M2;

(4) a composition (III) comprising (I);

(5) a kit (IV) comprising (I) and a control peptide, each in a container;

(6) an antibody (V) that selectively binds to (I);

(7) a method (M3) involving injecting a subject with a phage display library, recovering at least one sample of at least one organ, tissue or cell type, separating the sample into isolated cells or clumps of cells, centrifuging the cells through an organic phase to form a pellet and recovering phage from the pellet;

(8) a gene therapy vector (VI) which expresses (I) as part of a surface protein;

(9) identifying (M4) targeting peptides to angiogenic tissue involves inducing hypoxia in a neonatal subject, administering a phage display library to the subject and recovering phage from the retina of the subject;

(10) inducing (M5) apoptosis in a cell by attaching Annexin V to a permeabilizing agent to form a complex and administering the complex to the cell;

(11) modulating (M6) angiogenesis by obtaining a peptide comprising at least 3 contiguous amino acids selected from 39 sequences given in the specification and administering the peptide to a subject; and

(12) detecting (M7) receptors for endostatin or angiostatin by obtaining a sample from a tissue or organ, incubating the sample with endostatin or angiostatin and detecting the presence of endostatin or angiostatin bound to the sample.

ACTIVITY - Cytostatic; Anorectic; Contraceptive.

MECHANISM OF ACTION - Inducer of apoptosis in a cell; modulator of angiogenesis (claimed); inhibitor of tumor growth; inhibitor of pregnancy; inducer of weight loss. No supporting data is given.

USE - (I) is useful in a method for interfering with pregnancy by administering (I) to a female subject, for delivering an agent to fetus by attaching (I) to an agent and administering (I) to a pregnant subject, for targeting delivery to adipose tissue by attaching (I) to an agent to form a complex and administering the complex to a subject, for targeting delivery to organ or tissue by attaching (I) to an agent and administering the agent to a subject, for targeting delivery to prostate cancer or angiogenic tissue by attaching (I) to a therapeutic agent to form a complex and administering the complex to a subject, for diagnosing prostate cancer by administering (I) to a subject suspected of having prostate cancer and detecting (I) bound to prostate cancer cells, and for inducing apoptosis in a cell by attaching (I) to a permeabilizing agent to form a complex and administering the complex to the cell (claimed). (I) is useful therapeutically for inhibiting angiogenesis, inhibiting tumor growth, inducing apoptosis, inhibiting pregnancy inducing weight loss, and for treating a disease state. (I) is useful for imaging and diagnosis of various diseased organs, tissues or cell types.

Dwg.0/31

L10 ANSWER 8 OF 24 WPIDS (C) 2003 THOMSON DERWENT

AN 2002-356509 [39] WPIDS

DNC C2002-101517

TI Matrix **metalloprotease inhibitor** for use in pharmaceuticals and cosmetics for preventing aging of skin, contains extract of *Lonicera gracilipes* var.gladra.

DC B04 D21

PA (FANK-N) FANKERU KK

CYC 1

PI JP 2002/047133 A 2002/02/12 (200239)* 6p

ADT JP 2002047133 A JP 2000-230166 20000731

PRAI JP 2000-230166 20000731

AB JP2002047133 A UPAB: 20020621

NOVELTY - A matrix **metalloprotease inhibitor** contains an extract of *Lonicera gracilipes* var.gladra.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a pharmaceuticals containing extract of *Lonicera gracilipes* var.gladra;

(2) a cosmetics containing extract of *Lonicera gracilipes* var.gladra;

(3) skin external preparation containing extract of *Lonicera gracilipes* var.gladra; and

(4) an anti-aging agent containing extract of *Lonicera gracilipes* var.gladra.

ACTIVITY - Dermatological.

Biological data not given in source material.

NPA

MECHANISM OF ACTION - Matrix metalloprotease (MMP) inhibitor.

The matrix metalloprotease inhibitory effect of extract of *Lonicera gracilipes* var. *glabra* was measured according to the method E.Harris et.al. (MethodEnzymol., 82, 423, 1982) using human fibroblast origin MMP-1. The extract was added with type-II collagen and isothiocyanate and tris-hydrochloric acid buffer containing sodium chloride and calcium chloride. The mixture was incubated for 3 hours at 37 deg. C. The reaction was stopped using tris-hydrochloric acid buffer containing sodium chloride, O-phenanthroline and ethanol. The mixture was centrifuged for 15 minutes and the fluorescence intensity of the liquid was measured at 485 nm. The result showed that the 50% inhibitory concentration (IC50) value of the extract was 0.33 mg/ml.

USE - As cosmetics and pharmaceuticals for preventing aging such as cream, lotion, ointment, lip stick, eye color and cheek color.

ADVANTAGE - The matrix metalloprotease inhibitor has excellent anti-aging effect.
Dwg. 0/0

L10 ANSWER 9 OF 24 WPIDS (C) 2003 THOMSON DERWENT

AN 2002-154611 [20] WPIDS

DNC C2002-048298

TI Treating or preventing cancer, such as basal cell carcinoma, comprises administering immunostimulatory nucleic acids that induce expression of cell surface antigens and antibodies to a subject having or at risk of developing cancer.

DC B02 B03 B04 D16

IN HARTMANN, G; WEINER, G

PA (IOWA) UNIV IOWA RES FOUND

CYC 95

PI WO 2001097843 A2 20011227 (200220)* EN 220p

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
NL OA PT SD SE SL SZ TR TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU
SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW

AU 2001070134 A 20020102 (200230)

ADT WO 2001097843 A2 WO 2001-US20154 20010622; AU 2001070134 A AU 2001-70134 20010622

FDT AU 2001070134 A Based on WO 200197843

PRAI US 2000-213346P 20000622

AB WO 200197843 A UPAB: 20020402

NOVELTY - Methods for treating or preventing cancer comprising administering to a subject having or at risk of developing cancer, immunostimulatory nucleic acids that induce expression of cell surface antigens and antibodies, are new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are provided for the following:

(1) a method (M1) for treating or preventing cancer, comprising administering to a subject having or at risk of developing cancer, an effective amount of a nucleic acid that upregulates CD20 expression, and an anti-CD20 antibody;

(2) a method (M2) for diagnosing lymphoma, comprising isolating a B cell from a subject having or suspected of having a type of lymphoma and identifying a change in a cell surface marker when the B cell is contacted with an immunostimulatory nucleic acid, wherein the cell surface marker induced on the B cell is indicative of the type of lymphoma;

(3) a method (M3) for treating or preventing cancer, comprising administering to a subject having or at risk of developing cancer, an effective amount of a nucleic acid to induce expression of a surface antigen on a cancer cell surface, and administering to the subject an antibody selected from an anti-CD22 antibody or an anti-CD19 antibody;

(4) a method (M4) for treating lymphoma, comprising isolating a B cell from a subject having lymphoma, identifying a surface antigen which is not expressed or which is expressed on the surface of the B cell in an

amount lower than that of a control B cell, administering to the subject an antibody specific for the identified surface antigen and an immunostimulatory nucleic acid in order to treat the cancer, wherein the immunostimulatory nucleic acid is administered in an effective amount to upregulate expression of the surface antigen on the cancer cell surface;

(5) a method (M5) for treating a lymphoma resistant to antibody therapy, comprising administering to a subject having a lymphoma resistant to therapy with an antibody specific for a surface antigen, an antibody specific for the surface antigen to which the lymphoma is resistant and a nucleic acid in order to treat the lymphoma, wherein the nucleic acid is administered in an effective amount to upregulate expression of the surface antigen on the lymphoma cell surface;

(6) a method (M6) for treating cancer in a human, comprising administering to a human an immunostimulatory nucleic acid and an antibody of IgG1 isotype, which binds to a cell surface antigen of a cancer cell and wherein the nucleic acid and the antibody are administered in an effective amount for killing the cancer cell; and

(7) a kit, comprising a package including at least two containers, the first container housing an immunostimulatory nucleic acid, the second container housing an antibody specific for a cell surface antigen, and instructions for screening a cell to determine whether the immunostimulatory nucleic acid upregulates expression of the cell surface antigen.

ACTIVITY - Cytostatic.

Mice were injected intraperitoneally (i.p.) with 5000 T3C cells on day 0. They were then given 100 micrograms anti-idiotypic monoclonal antibody as either IgG1 (MS5A10) or IgG2a (MS11G6) on days 5, 7, and 10. In this model, the target antigen was the idiotype expressed by the lymphoma cells. Therefore, the anti-tumor antibodies were also 'anti-idiotypic'. These antibodies (MS5A10 and MS11G6) were simultaneously both anti-tumor antibodies and anti-idiotypic antibodies. Twenty micrograms of CpG nuclease resistant phosphorothiate-modified oligodeoxynucleotide (ODN) 1826 (5'-TCCATGACGTTCCCTGACGTT-3') was given at the same time. Untreated controls had a median survival time (MST) of 17 days after inoculation with tumor. Mice treated with murine IgG1 antibody plus CpG ODN had survival that was similar to those treated with murine IgG1 antibody alone (MST 28 days and 27 days, respectively). In contrast, mice treated with murine IgG2a plus CpG ODN had survival that was significantly improved when compared to mice treated with murine IgG2a alone (MST 45 days and 37 days, respectively).

MECHANISM OF ACTION - The immunostimulatory nucleic acid molecules induce the expression of cell surface antigens such as CD20 on the surface of the cancer cell. The induction of these antigens leads to enhanced antibody-dependent cellular cytotoxicity (ADCC).

USE - The methods are useful for treating or preventing cancer such as basal cell carcinoma, bladder cancer, bone cancer, brain and central nervous system (CNS) cancer, breast cancer, cervical cancer, colon and rectum cancer, connective tissue cancer, esophageal cancer, eye cancer, kidney cancer, larynx cancer, leukemia, liver cancer, lung cancer, Hodgkin's lymphoma, non-Hodgkin's lymphoma, melanoma, myeloma, oral cavity cancer (e.g., lip, tongue, mouth, and pharynx), ovarian cancer, pancreatic cancer, prostate cancer, rhabdomyosarcoma, skin cancer, stomach cancer, testicular cancer, and uterine cancer.

Dwg.0/6

L10 ANSWER 10 OF 24 WPIDS (C) 2003 THOMSON DERWENT
AN 2002-066668 [09] WPIDS
DNC C2002-019916
TI New hydroxamic acid derivatives are e.g. matrix metalloproteinase inhibitors useful for treating e.g. cancer, inflammation, autoimmune, infectious or ocular disease.
DC B05
IN BAXTER, A D; DYKE, H J; HANNAH, D R; SHARPE, A
PA (DARW-N) DARWIN DISCOVERY LTD; (BAXT-I) BAXTER A D; (DYKE-I) DYKE H J; (HANN-I) HANNAH D R; (SHAR-I) SHARPE A

CYC 96

PI WO 2001087870 A1 20011122 (200209)* EN 54p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU
SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW

AU 2001058540 A 20011126 (200222)

US 2002037900 A1 20020328 (200225)

ADT WO 2001087870 A1 WO 2001-GB2151 20010515; AU 2001058540 A AU 2001-58540
20010515; US 2002037900 A1 US 2001-858106 20010515

FDT AU 2001058540 A Based on WO 200187870

PRAI GB 2000-29393 20001201; GB 2000-11721 20000515

AB WO 200187870 A UPAB: 20020208

NOVELTY - Hydroxamic acid derivatives (I) or their salts, solvates, hydrates, N-oxides, protected amino, protected carboxy derivatives are new.

DETAILED DESCRIPTION - Hydroxamic acid derivatives of formula D-B-X-A-S(O)2-CH2C(R3)(R2)-C(O)-NHOH (I) or their salts, solvates, hydrates, N-oxides, protected amino, protected carboxy derivatives are new.

R2 = H, alkyl, alkenyl, alkynyl, (aryl)alkyl, heteroaryl, heteroarylalkyl, cycloalkyl, cycloalkylalkyl, heterocyclo, heterocycloalkyl or cycloalkyl (all are optionally substituted by T);

T = R4, W or WR4;

R3 = H or alkyl; or

CR2R3 = carbocyclic or heterocyclic ring (optionally substituted by T);

A = heterocyclic ring (attached to SO2 through a nitrogen atom) (optionally substituted by R4);

B = (hetero)aryl ring (optionally substituted by R5);

D = (hetero)aryl ring (optionally substituted by R5); or heterocyclic ring attached through a carbon atom (optionally substituted by R4 at any available C or with R14 at any available nitrogen atom);

R4 = Q, =O or =NOR10;

Q = OR6, COR10, CO2R9, CONR7R8, NR10R11, S(O)qR10, S(O)qNR7R8 or CN;

R5 = (cyclo)alkyl, CF3, halo or Q;

R6 = H, T1, CF3, CHF2 or CH2F;

T1 = (cyclo)alkyl, (hetero)aryl, heterocyclo, (hetero)arylalkyl, heterocycloalkyl or cycloalkylalkyl;

R7, R8 and R10 = H or T1; or

NR7R8 = heterocyclic ring;

R9 = H or (cyclo)alkyl;

R11 = H, T1, COR12, CONR7R8, S(O)qR12 or S(O)qNR7R8; or

NR10R11 = heterocyclic ring optionally substituted by R13;

R12 = OR6 or R13;

R13 = T1;

R14 = H or (cyclo)alkyl;

q = 0 - 2;

W = T1;

X = -O-, -CO-, S(O)q-, -N(R10), or is absent;

provided that both B and D are not phenyl; and that R4 is not =O or =NOR10, if it is a substituent on an aromatic ring.

ACTIVITY - Cytostatic; antiallergic; antiinflammatory; nootropic; neuroprotective; immunosuppressive; antiasthmatic; antiarteriosclerotic; antibacterial; vulnerary; immunomodulator; cerebroprotective; dermatological; antidiabetic; ophthalmological; anticoagulant; gynecological; antipyretic; cardiant; hemostatic; anti-HIV; vasotropic; antimigraine; osteopathic; antiarthritic; antipsoriatic; antirheumatic; antiskling; thrombolytic; antiulcer.

MECHANISM OF ACTION - Matrix metalloproteinase inhibitor; ADAM or ADAM-TS enzyme (mammalian metalloproteinase) inhibitor.

No details of tests are given.

USE - For the manufacture of a medicament for the treatment of cancer, inflammation, autoimmune, infectious or ocular disease (e.g. neovascularization), graft versus host reactions, psoriasis, atopic dermatitis, rhinitis, eczema, systemic lupus erythematosus, solid organ transplant, cystic fibrosis, rheumatoid arthritis, osteoarthritis, osteoporosis, Crohn's disease, ulcerative colitis, multiple sclerosis, periodontitis, bone resorption, bacterial infections, epidermolysis bullosa, tumor growth, angiogenesis, ophthalmological disease, retinopathy, asthma, emphysema, bronchitis, chronic obstructive pulmonary disease (COPD), diabetic retinopathy, retinopathy or prematurity or age-related macular degeneration (all claimed); in human or veterinary medicine; for treatment or prophylaxis of diseases or conditions mediated by MMPs such as cardiovascular diseases, diseases involving tissue breakdown, neurodegeneration, Alzheimer's disease, stroke, vasculitis, gingivitis, hemorrhage, coagulation, acute phase response, cachexia, anorexia, acute infections, bacterial infections; HIV infections, fever, shock states, dermatological conditions, surgical wound healing, invasion by secondary metastases, corneal ulceration, reperfusion injury, migraine, meningitis, allergic conjunctivitis, anaphylaxis, restenosis, congestive heart failure, endometriosis, atherosclerosis, endosclerosis, aspirin-independent anti-thrombosis; pelvic inflammatory disease (PID), cancer induced bone resorption, lung diseases e.g. cystic fibrosis, adult respiratory distress syndrome (ARDS), bronchitis obliterans-organizing pneumonia (BOOP), idiopathic pulmonary fibrosis (PIF), diffuse alveolar damage, pulmonary Langerhan's cell granulomatosis, pulmonary lymphangiioleiomyomatosis (LAM), periodontitis, chronic glaucoma, retinal detachment, retinopathy of prematurity (ROP), sickle cell retinopathy, chronic uveitis, neoplasm (retinoblastoma, pseudoglioma), Fuch's heterochromic iridocyclitis, Sorsby's maculopathy, neovascular glaucoma, corneal neovascularization, neovascularization following a combined vitrectomy and lensectomy, retinal ischemia, choroidal vascular insufficiency, choroidal thrombosis, carotid artery ischemia, neovascularization of the optic nerve and neovascularization due to penetration of the eye or contusive ocular injury such as traumatic disciform lesions.

ADVANTAGE - (I) exhibits in vitro inhibition activity with respect to the MMP (matrix metalloproteinase) enzymes).
Dwg.0/0

L10 ANSWER 11 OF 24 WPIDS (C) 2003 THOMSON DERWENT
AN 2002-055319 [07] WPIDS
DNC C2002-015790
TI Treating conjunctival bleb and optic nerve damage following glaucoma filtering surgery and ischemic damage to retina and optic nerve comprises administering matrix metalloproteinase inhibitor.
DC B05
IN CHINTALA, S K; FINI, M E; SCHUMAN, J S
PA (NEWE-N) NEW ENGLAND MEDICAL CENT HOSPITALS INC; (CHIN-I) CHINTALA S K; (FINI-I) FINI M E; (SCHU-I) SCHUMAN J S
CYC 95
PI WO 2001080862 A1 200111/01 (200207)* EN 38p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ
LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD
SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
AU 2001057272 A 20011107 (200219)
US 2002042402 A1 20020411 (200227)
US 6503892 B2 20030107 (200306)
ADT WO 2001080862 A1 WO 2001-US13368 20010426; AU 2001057272 A AU 2001-57272 20010426; US 2002042402 A1 Provisional US 2000-199881P 20000426, US 2001-841936 20010425; US 6503892 B2 Provisional US 2000-199881P 20000426, US 2001-841936 20010425

FDT AU 2001057272 A Based on WO 200180862
 PRAI US 2001-841936 20010425; US 2000-199881P 20000426
 AB WO 200180862 A UPAB: 20020130
 NOVELTY - Treating or preventing leakage of a conjunctival bleb and treating or preventing optic nerve damage in the **eye** of a subject who has undergone glaucoma filtering surgery and treating ischemic damage to the **retina** and optic nerve comprises administration of a matrix **metalloproteinase inhibitor**.
 ACTIVITY - Ophthalmological.
 MECHANISM OF ACTION - Matrix metalloproteinase (MMP) inhibitor.
 In a test using adult CD-1 mice, 60 minutes of **retinal** ischemia caused 25-30% **retinal** ganglion cell loss. No loss was observed in MMP-9 knockout mice.
 USE - Used for treating or preventing leakage of a conjunctival bleb and treating or preventing optic nerve damage in the **eye** of a subject who has undergone glaucoma filtering surgery and treating ischemic damage to the **retina** and optic nerve.
 Dwg.0/11

L10 ANSWER 12 OF 24 WPIDS (C) 2003 THOMSON DERWENT
 AN 2001-616269 [71] WPIDS
 DNC C2001-184482

TI Treating and preventing ophthalmological disorders e.g. **retinal** neovascularization comprises administering composition comprising therapeutic agent e.g. hydroxamic acid, and optionally polymeric suspension agent.

DC A96 B05 D16
 IN BOWMAN, L M; ROWE-RENDLEMAN, C; ROY, S; SI, E C
 PA (INSI-N) INSITE VISION INC
 CYC 94
 PI WO 2001068053 A2 20010920 (200171)* EN 50p

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
 NL OA PT SD SE SL SZ TR TZ UG ZW
 W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM
 DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC
 LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE
 SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW

AU 2001040066 A 20010924 (200208)
 KR 2001113918 A 20011228 (200240)
 EP 1261317 A2 20021204 (200280) EN
 R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
 RO SE SI TR

ADT WO 2001068053 A2 WO 2001-US7171 20010307; AU 2001040066 A AU 2001-40066
 20010307; KR 2001113918 A KR 2001-714259 20011108; EP 1261317 A2 EP
 2001-914710 20010307, WO 2001-US7171 20010307

FDT AU 2001040066 A Based on WO 200168053; EP 1261317 A2 Based on WO 200168053
 PRAI US 2000-648446 20000828; US 2000-523102 20000310
 AB WO 200168053 A UPAB: 20011203

NOVELTY - Treating and preventing ophthalmological disorders comprises topically administering to the **eye** a composition delivering a therapeutic agent (I) to the posterior segment of the **eye**. The composition optionally includes a polymeric suspension agent (II).

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for a topical composition comprising (I) and optionally (II).

ACTIVITY - Ophthalmological.

Tests are described, but no relevant results are given.

MECHANISM OF ACTION - None given.

USE - Used for treating ophthalmic disorders, preferably posterior segment ophthalmic disorders, particularly **retinal** neovascularization (claimed), macular degeneration, diabetic retinopathy, retinopathy of prematurity, retinitis pigmentosa, macular edema, glaucoma, posterior uveitis, endophthalmitis, ocular insult and ocular manifestation of systemic disease e.g. viral infection, arthritis and rosacea.

ADVANTAGE - The composition may be self administered without using anesthetics to deliver therapeutically effective amounts of active agent.

NPA

Dwg.0/5

L10 ANSWER 13 OF 24 WPIDS (C) 2003 THOMSON DERWENT
AN 2001-586154 [66] WPIDS
DNC C2001-173702
TI New composition for matrix **metalloproteinase inhibitor**
comprises hyaluronic acid polysulfate or dermatan polysulfate.
DC B04
PA (MARU-N) MARUHO KK
CYC 1
PI JP 2001163789 A 20010619 (200166)* 6p
ADT JP 2001163789 A JP 1999-353028 19991213
PRAI JP 1999-353028 19991213
AB JP2001163789 A UPAB: 20011113
NOVELTY - New composition for matrix metalloproteinase (MMP) inhibitor
comprises at least one substance selected from hyaluronic acid
polysulfate, dermatan polysulfate or their salts.
ACTIVITY - Antiinflammatory; dermatological; cytostatic;
ophthalmological; antiulcer.
No biological data given.
MECHANISM OF ACTION - MMP (matrix **metalloproteinase**)
inhibitor.
To fluorescence labeled substrate solution was added MMP-3 derived
from human ulcerative cells to carry our enzyme reaction, and fluorescent
intensity (520 nm) of the substrate decomposed product (erected
wavelength:495 nm) was measured. Hyaluronic acid polysulfate and dermatan
polysulfate were added to the reaction solution, adjusting at 10⁻⁷ M
respectively, and MMP-3 inhibitory activity of each sample was evaluated.
The results showed that hyaluronic acid polysulfate (10⁻⁷ M concentration)
inhibited MMP-3 activity by 20 % and dermatan polysulfate did by 50 %.
USE - The composition is for the prevention or treatment of various
diseases accompanied by decomposition of extracellular matrix. Various
diseases are dermal disorder such as injury; or ulcerative, bullosus,
granulomatous and lichenoid dermatitis; or **eye** disorder such as
corneal ulcer and retinopathy. Injury or ulcerative dermatitis is wound,
burn, chronic ulcer, decubital ulcer, pyogenic granuloma or dermal
disorder caused by sunshine. Bullosus, granulomatous or lichenoid dermal
disorder is pemphigus, porphyria cutanea tarda, epidermolysis bullosa
dystrophica, epidermolysis bullosa hereditaria simplex, dermatitis
herpetiformis, erysipelas, pompholyx, granuloma annulare, necrobiosis
lipoidica diabetorum or lichen planus (all claimed).
The composition is used as MMP inhibitor, and effective for the
prevention and treatment of inflammatory disorder, dermal disorder,
cancer, circulatory disorder, **eye** disorder or nerve inflammatory
disorder.
ADVANTAGE - The compound is safe and has a different structure from
the conventional MMP inhibitors.

Dwg.0/1

L10 ANSWER 14 OF 24 WPIDS (C) 2003 THOMSON DERWENT
AN 2001-514501 [56] WPIDS
DNC C2001-153732
TI Composition comprising a combination of an oxidizing and/or reducing
agent, a protein-denaturing agent, and a hapten, useful for treating
neoplasms, tumors, and cancers.
DC B05 D16
IN YU, B
PA (YUBB-I) YU B
CYC 94
PI WO 2001052868 A1 20010726 (200156)* EN 83p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM
DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC
LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE

US Case
a type

SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW

AU 2001030977 A 20010731 (200171)

US 2002044919 A1 20020418 (200228)

ADT WO 2001052868 A1 WO 2001-US1737 20010118; AU 2001030977 A AU 2001-30977
20010118; US 2002044919 A1 Provisional US 2000-177024P 20000119, US
2001-765060 20010117

FDT AU 2001030977 A Based on WO 200152868

PRAI US 2000-177024P 20000119; US 2001-765060 20010117

AB WO 200152868 A UPAB: 20011001

NOVELTY - A composition (I) comprising a combination of an oxidizing or reducing agent, a protein-denaturing agent, and a hapten, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a kit comprising the combination (I);

(2) an article of manufacture comprising:

(a) packaging material;

(b) the combination above; and

(c) a label indicating that the article is for treating neoplasms;

and

(3) a method for treating neoplasm in a mammal comprising in situ administration to the neoplasm of a mammal, a hapten and a coagulation agent or treatment that causes coagulation of the neoplasm (an autologous immune response is generated against the neoplasm).

ACTIVITY - Cytostatic.

31 advanced stage IV liver cancer patients were treated using the new combination. Prior to procedure, patients were given a mild sedative or painkiller. Patients were calmed thoroughly and were also monitored by modern medial imaging. With local anesthesia, percutaneous puncture was administered directly into the tumor using a spinal needle connected to a high-power syringe containing a combination of ethanol, H2O2, anticancer drug AraC (8 mg/ml) and hemotoxilin (5 mg/ml). Combination was injected directly into the tumor and distributed throughout the matrix of the whole tumor. Sonic imaging showed the stranger echo imaging which indicated the coagulation area.

Following coagulation lysis and tumor cell death monitored by sonic imaging, which showed liquefied echo, tumor started to shrink and disappear. Normal tissues grew replacing the tumor. The process was monitored by medical imaging systems. The amount of the ingredients of the combination injected into the tumor was determined by the diameter of tumors (cm) with 2 ml of the combination for each centimeter.

Procedure was repeated in 1-2 weeks. On average, each patient was treated with the injection for 3 times. No severe side effects for all the treated patients was observed, although some patients experienced tolerable pain the injection site while a few had light fever during the first week. All side effects disappeared in about 1 week. No serious complications happened in any cases.

MECHANISM OF ACTION - Gene therapy.

USE - The combination and the methods are useful for treating neoplasms, tumors, and cancers, including neoplasm or cancer of the e.g. adrenal gland, anus, auditory nerve, bile ducts, bladder, bone, brain, breast, bruccal, central nervous system, cervix, colon, ear, endometrium, esophagus, eye, eyelids, fallopian tube, gastrointestinal tract, head and neck, heart, kidney, larynx, liver, lung, or mandible.

The combination and methods may further be used in treating tumors of mesenchymal origin (e.g. connective tissue and derivatives, or endothelial and related tissues blood vessels), epithelial origin (stratified squamous carcinoma, or basal cells of skin or adenexa), and tumors derived from more than one neoplastic cell types derived from more than one germ layers.

The treatment may be used with radiation therapy, before surgery for the pre-treatment of neoplasm for easier removal of the neoplastic mass and reduces the neoplasm metastasis rate, or with gene therapy.

Dwg.0/4

AN 2001-451774 [48] WPIDS
DNN N2001-334447 DNC C2001-136453
TI Plaque for intravitreal administration for treating intraocular conditions such as retinopathies, comprises inner and outer surfaces, and one or more guide units for guiding needle into interior portion of eye.
DC B07 P32
IN BILLSON, F A; GILLIES, M C; PENFOLD, P L
PA (UNSY) UNIV SYDNEY
CYC 95
PI WO 2001049226 A1 20010712 (200148)* EN 20p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM
DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC
LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE
SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001026527 A 20010716 (200169)
EP 1253892 A1 20021106 (200281) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
RO SE SI TR
ADT WO 2001049226 A1 WO 2001-AU12 20010108; AU 2001026527 A AU 2001-26527
20010108; EP 1253892 A1 EP 2001-901015 20010108, WO 2001-AU12 20010108
FDT AU 2001026527 A Based on WO 200149226; EP 1253892 A1 Based on WO 200149226
PRAI AU 2000-4965 20000106
AB WO 200149226 A UPAB: 20010829
NOVELTY - A plaque (5) positioned over a patient's eye, .
comprises an inner surface which contacts the anterior surface of the
eye, and an outer surface positioned which faces away from the
eye. The inner surface has surface area equivalent to the exposed
surface of the eye. The plaque is further provided with one or
more guide units (6b), for guiding a needle into the interior of
eye (pars plana). *not topical*
DETAILED DESCRIPTION - The guide units are placed at a distance from
the plaque which corresponds to center of iris. The plaque has a pair of
opposed retaining units directed and dimensioned to ensure retraction of
eye lids, when the plaque is placed over the eyes. The
plaque has a control unit on the outer surface which regulates the
penetration of needle into the eye. INDEPENDENT CLAIMS are also
included for the following:
(1) kit for use in intraocular injection of compound; and
(2) guiding and administering an intraocular composition into the
interior of a patient's eye.
USE - Useful for intravitreal administration of therapeutic agents,
for treating intraocular conditions such as variety of exudative,
edematous and inflammatory retinopathies such as macular degeneration,
diabetic retinopathy, diabetic macular edema, cystoid macular edema,
uveitis, endophthalmitis, retinal veno-occlusive disease,
proliferative vitreo retinopathy, iritis, photodynamic therapy for macular
degeneration, and also for application to aphakic eye.
ADVANTAGE - The plaque effectively immobilizes both the eye
and eyelids during intraocular injection, prevents indentation of
eye surface by penetration of needle and also allows correct angle
of attack by needle, suitably at a distance from limbus and at suitable
depth.
DESCRIPTION OF DRAWING(S) - The figure shows the illustration of the
plaque in position over the eye with a needle being introduced
through one of the guide unit.
Syringe 1
Needle 2
Plaque 5
Guide units 6b
Dwg.4/6

AN 2001-441715 [47] WPIDS

DNC C2001-133464

TI Novel isolated expression vector useful therapeutically, comprises silencer elements and conditionally inducible elements to form silencer-inducible region, and a promoter in operative linkage with the region.

DC B04 D16

IN WEBSTER, K A

PA (UYMI-N) UNIV MIAMI

CYC 28

PI WO 2001048187 A2 20010705 (200147)* EN 48p

RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR

W: CA JP

EP 1242592 A2 20020925 (200271) EN

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
RO SE SI TR

ADT WO 2001048187 A2 WO 2000-US33269 20001215; EP 1242592 A2 EP 2000-984041
20001215, WO 2000-US33269 20001215

FDT EP 1242592 A2 Based on WO 200148187

PRAI US 2000-723326 20001128; US 1999-171597P 19991223

AB WO 200148187 A UPAB: 20010822

NOVELTY - An expression vector (I) comprising silencer elements and conditionally inducible elements to form a silencer-inducible region (IR), and a promoter (P) in operative linkage with IR, where (P) is regulated by IR, and upstream of the expressed region, and (I) under an inducing condition expresses downstream region (DR) in an amount greater than expression of DR without inducing condition, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a genetically engineered cell or non-human organism (II) containing (I) which was introduced into a host cell or non-human organism;

(2) production of (I);

(3) an isolated polynucleotide (III) comprising a silencer-inducible region comprising a silencer element and a conditionally inducible element, where the conditionally inducible element is operably linked to an heterologous to the silencer element, where operably linking the silencer-inducible region to a promoter provides for conditional silencing of transcription from the promoter; and

(4) an expression vector (IV) comprising (III).

ACTIVITY - Vasotropic; antiallergic; antianemic; immunosuppressive; antiinflammatory; cytostatic; anti-HIV; hemostatic.

Exposure of cardiac myocytes to hypoxia for 24 hours (hr) and reoxygenation for 20 hr caused death by apoptosis of greater than 30% of the myocytes. This model was used to determine whether a hypoxia-activated gene (e.g., DT-diaphorase) that was silenced under aerobic conditions could protect cardiac myocytes from the oxidative stress caused by hypoxia-reoxygenation. DT-diaphorase is an antioxidant that mediates quenching of free radicals that are generated by quinone cycling during mitochondrial electron transport.

A cDNA insert encoding DT-diaphorase was removed from a pcDNA vector with HindIII. The about 1.3 kb insert was cloned into the HindIII-XbaI restriction enzyme sites of pGLPV-(HRE/SIL)3 after removing the luciferase cDNA insert. This was done by ligating at the HindIII restriction enzyme site and filling in the remaining cohesive ends and blunt end circularizing.

The construct was called pGLPV-(HRE/SIL)3-DT-d. Cardiac myocytes were transfected with 2 μ g of a CMV-green fluorescent protein (GFP) and 8 μ g of pGLPV-(HRE/SIL)3-DT-d or empty vector as the control. Transfected cultures were exposed to hypoxia-reoxygenation to cause 30% cell apoptosis. Parallel cultures were treated with 1% H₂O₂ to induce oxidative stress without hypoxia.

The results showed that cells transfected with pGLPV-(HRE/SIL)3-DT-d were strongly protected against apoptosis caused by 24 hr hypoxia and 20 hr reoxygenation. Control cultures transfected with empty vector displayed

24% apoptosis of GFP-positive cells after reoxygenation.

MECHANISM OF ACTION - Gene therapy.

USE - (I) is useful diagnostically, therapeutically, prophylactically or to make models of human disease. (I) is useful in gene therapy, production of recombinant biologicals, genetic diagnosis, drug screening, and genetic research (e.g., genomics, proteomics, in vivo and in vitro models of human disease).

(I) is useful for treating cardiac disease (by reduction or prevention of ischemic damage, inhibition of restenosis, neutralization of other pathological effects of heart or vascular disease, or diagnosis of hypoxia), acquired or inherited immunodeficiency, allergy, anemia, thalassemia, autoimmune disease, hemolytic or septic shock, hemophilia, inflammation and other stress conditions, ischemia and other hypoxic conditions, carcinoma, leukemia, Hodgkin disease, non-Hodgkin lymphoma and Kaposi sarcoma. (I) is useful for suppressing or eliminating infectious agents, autoimmune cells and cancerous cells, and for preventing an infection or disease in a patient.

Dwg.0/3

L10 ANSWER 17 OF 24 WPIDS (C) 2003 THOMSON DERWENT
AN 2000-195436 [17] WPIDS
CR 2002-625807 [67]
DNC C2000-060662
TI Intrascleral injection for therapeutic or diagnostic material to posterior segment of the eye.
DC B07 D16 P31 P32 P34
IN BOWMAN, L M; CLARK, L A; HECKER, K I; PFEIFFER, J F; HECKER, K L
PA (INSI-N) INSITE VISION INC
CYC 87
PI WO 2000007565 A2 20000217 (200017)* EN 33p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL
OA PT SD SE SL SZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB
GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU
LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR
TT UA UG UZ VN YU ZA ZW
AU 9953327 A 20000228 (200030)
NO 2001000556 A 20010403 (200128)
EP 1100462 A2 20010523 (200130) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
RO SE SI
US 6378526 B1 20020430 (200235)
JP 2002522373 W 20020723 (200263) 36p
ADT WO 2000007565 A2 WO 1999-US17543 19990802; AU 9953327 A AU 1999-53327
19990802; NO 2001000556 A WO 1999-US17543 19990802, NO 2001-556 20010201;
EP 1100462 A2 EP 1999-938953 19990802, WO 1999-US17543 19990802; US
6378526 B1 US 1998-127920 19980803; JP 2002522373 W WO 1999-US17543
19990802, JP 2000-563251 19990802
FDT AU 9953327 A Based on WO 200007565; EP 1100462 A2 Based on WO 200007565;
JP 2002522373 W Based on WO 200007565
PRAI US 1998-127920 19980803
AB WO 200007565 A UPAB: 20021022
NOVELTY - Intrascleral injection comprises injecting into the scleral layer of an eye through a location on the exterior surface of the sclera that overlies retinal tissue an effective amount of a therapeutic or diagnostic material
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for:
(A) a method for treating posterior ocular tissue comprising forming a depot of a therapeutic material within the sclera of an eye at a location that overlies retinal tissue, in which the therapeutic material diffuses over time through the sclera and into the underlying tissue or tissues in an effective amount;
(B) a method for treating ocular tissue comprising propelling a diagnostic or therapeutic material through at least a portion of a scleral layer and into at least the underlying choroidal or retinal

tissue.

ACTIVITY - Antiinflammatory; Antidiabetic; Ophthalmological.

MECHANISM OF ACTION - **Metalloproteinase-Inhibitor**
; VEGF-Regulator; Protein-Kinase-Inhibitor-C; NMDA-Antagonist;
AMPA-Antagonist; Calcium-Channel-Blocker.

USE - The methods can be used for treating an **eye** suffering from an ocular disease such as cystoid macular edema, age-related macular degeneration, diabetic retinopathy, diabetic maculopathy, central **retinal** artery occlusion, central **retinal** vein occlusion, branch **retinal** artery occlusion, branch **retinal** vein occlusion, retinopathy of prematurity, sickle cell retinopathy, photic retinopathy, radiation retinopathy, **retinal** detachment, retinitis pigmentosa, macular hole, cataract and glaucoma (claimed).

ADVANTAGE - Intrasccleral injection of a therapeutic or diagnostic material at a location overlying the **retina** provides a minimally invasive technique for delivering the agent to the posterior segment of the **eye**. The procedure allows for close proximity of the material to the targeted site. The sclera can be used to hold a depot of the material such as for sustained release or as a conduit for propelling material through whereby the material is delivered immediately to the underlying tissues but without physically penetrating the sclera with an instrument or otherwise unreasonably traumatizing the **eye**.

Dwg.0/1

L10 ANSWER 18 OF 24 WPIDS (C) 2003 THOMSON DERWENT

AN 2000-171129 [15] WPIDS

DNC C2000-053233

TI Novel peptides useful for treating osteoarthritis, cancer, rheumatoid arthritis and multiple sclerosis.

DC B03 B04 B05

IN KRUMME, D; TSCHESCHE, H

PA (KRUM-I) KRUMME D; (TSCH-I) TSCHESCHE H

CYC 87

PI WO 2000002904 A1 20000120 (200015)* EN 43p

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL
OA PT SD SE SL SZ UG ZW

W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB
GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU
LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR
TT UA UG US UZ VN YU ZA ZW

AU 9950346 A 20000201 (200028)

EP 1095057 A1 20010502 (200125) EN

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
RO SE SI

JP 2002520333 W 20020709 (200259) 44p

ADT WO 2000002904 A1 WO 1999-EP4826 19990708; AU 9950346 A AU 1999-50346
19990708; EP 1095057 A1 EP 1999-934642 19990708, WO 1999-EP4826 19990708;
JP 2002520333 W WO 1999-EP4826 19990708, JP 2000-559133 19990708

FDT AU 9950346 A Based on WO 200002904; EP 1095057 A1 Based on WO 200002904;
JP 2002520333 W Based on WO 200002904

PRAI EP 1998-112652 19980708

AB WO 200002904 A UPAB: 20000323

NOVELTY - Matrix **metalloproteinase inhibitor** peptides containing the sequence Pro-Leu-Ama (NHOH)- are new.

DETAILED DESCRIPTION - Compounds containing aminomalononic acid derivatives and their peptide backbone modified derivatives of formulae (I)-(VI) and their salts are new:

R1 = N-protecting group (e.g. tert-butyloxycarbonyl), acetyl, Co-lower alkyl, CH2-aryl, natural amino acid, lower alkyl, aryl, H, or optionally spacer linked such as a synthetic or natural peptide, glycoprotein, a solid or macromolecular product used for chromatological procedures;

R2 = NH-D-C(Ph)-CH2, NH-L-C(Ph)-CH3, N(lower alkyl)2, NH-lower alkyl, NH-aryl, natural amino acid, lower alkyl ester of an amino acid, O-lower

ND

alkyl, NHOH or OH, or optionally spacer linked: such as synthetic or natural peptide, glycoprotein, solid or macromolecular product used for chromatographical procedures; or R4;

Ccc = optionally with abounded residue Rz; or Z;

R3 = lower alkyl or side chain of natural amino acid, or R4;

R7-R9 = H, alkyl, aryl, OH, CO-lower alkyl, O-lower alkyl, O-CH₂-aryl, O-aryl, or cyclopropyl, cyclopentyl, cyclohexyl, a 5- or 6-membered aromatic or aliphatic N-heterocyclic ring which is attached via the N-atom or via a C-atom and (a) optionally contains N, O and/or S as an additional ring member and (b) is optionally benzofused or optionally substituted on one or more other C-atoms by lower alkyl, aryl and/or oxo; or optionally spacer linked: such as synthetic or natural peptide, glycoprotein, solid or macromolecular product used for chromatographical procedures;

n = 0-5;

R10 = R2, R4 or (CH₂)_mR4;

m = 0-6;

R4 = H, alkyl, aryl, OH, O-lower alkyl, O-CH₂-aryl, O-aryl, NH-CO-aryl, NH-CO-NH-aryl, NH-CO-CH₂-aryl or NH-COR₅; NH₂, NH-lower alkyl, N(lower alkyl)₂, N(lower alkyl 1) (lower alkyl 2), NH aryl, N(aryl)₂, N(aryl 1) (aryl 2), N(lower alkyl)₃+, N(aryl₃); or cyclopropyl, cyclopentyl, cyclohexyl, a 5- or 6-membered aromatic or aliphatic N-heterocycle which is attached via the N-atom or via a C-atom and: (a) optionally contains N, O and/or S as an additional ring member, and (b) is optionally benzofused or optionally substituted on one or more other C-atoms by lower alkyl, aryl and/or oxo; or an optionally spacer linked: such as synthetic or natural peptide, glycoprotein, a solid or macromolecular product used for chromatographical procedures;

Z = OH, O-lower alkyl, NHOH, N(CH₃)OH, NHO-CH₃ or NHO-lower alkyl;

Q = (CH₂)_m, O-(CH₂)_m, CO(CH₂)_m, (CH₂)_mP, O-(CH₂)_m-P, or CO-(CH₂)_m-P;

P = cyclopropyl, cyclopentyl, cyclohexyl, 5- or 6-membered aryl, or a 5- or 6-membered aromatic or aliphatic N-heterocycle which is attached via the N-atom or via a C-atom and: (a) optionally contains N, O and/or S as an additional ring member, and (b) is optionally benzofused or optionally substituted on one or more other ring C-atoms by lower alkyl, aryl and/or oxo; lower = 1-6C; aryl = phenyl optionally substituted by lower alkyl, O-lower alkyl and/or halo; spacer = alkyl, amino alkyl, carboxyalkyl up to 12 C or combined forms, peptides or saccharides;

R₅ = R₁-proline, lower alkyl, aryl or cyclopropyl, cyclopentyl, cyclohexyl, a 5- or 6-membered aromatic or aliphatic N-heterocycle which is attached via the N-atom or via a C-atom, and: (a) optionally contains N, O and/or S, and (b) is optionally benzofused or optionally substituted on one or more other C-atoms by lower alkyl, aryl and/or oxo; or an optionally spacer linked: synthetic or natural peptide, glycoprotein, a solid or macromolecular product used for chromatographical procedures;

Aaa, Bbb = peptide bound natural amino acid;

Ccc = peptide bound natural amino acid or Thr (Bzl), Ser (Bzl) or NR₈C (QR₁₀)HCO;

R₆ = N-protecting group, acetyl, Co-alkyl(1-4C), natural amino acid, lower alkyl, H or R₁;

A-B, X-Y = CONH, CH₂NH, COCH₂, CH₂CH₂, CH₂S, CH₂O, CO-N (lower alkyl), CH₂-N(lower alkyl) or PHO₂-NH;

Any available H on any carbon or nitrogen in (I)-(VI) and any of the corresponding substituents may be in part or totally substituted by halo, alkyl, aryl, OH, CO-lower alkyl, O-lower alkyl, O-CH₂-aryl, O-aryl, or cyclopropyl, cyclopentyl, cyclohexyl, a 5 or 6-membered aromatic or aliphatic N-heterocycle which:

(a) contains N, O and/or S, and

(b) is optionally benzofused or optionally substituted on one or more other C-atoms by lower alkyl, aryl and/or oxo.

ACTIVITY - Osteopathic; Antirheumatic; Antiarthritic; Cytostatic; Neuroprotective; Antiinflammatory; Nootropic; Gastrointestinal-Gen.; Cerebroprotective; Hemostatic; Vulnery; Ophthalmological; Immunosuppressive; Respiratory-Gen.; Antilepemic; Gynecological.

MECHANISM OF ACTION - Matrix-Metalloproteinase-

Inhibitor. Compound (A) exhibited Ki values of 5×10^{-9} M for MMP-9 and 1.9×10^{-6} for dmMMP-8, respectively.

USE - The compounds are matrix **metalloproteinase inhibitors** useful for treating degenerative joint diseases, rheumatoid arthritis, osteoarthritis, cancer, metastasis, tumor invasion, multiple sclerosis, paradontosis, fibrosis, Alzheimer's disease, inflammatory bowel disease, neurodegenerative diseases, cerebral hemorrhage, wound healing, degenerative **eye** disease, aneurysm, artificial joint replacement, organ transplantation, emphysema, cholesteatoma and pre-eclampsia (claimed).

ADVANTAGE - The peptide nature of the inhibitors makes them similar to natural substances. However, in spite of the peptide character of the inhibitors, the P1-P1 peptide bond shows a high resistance to cleavage by proteinases.

Dwg.0/1

L10 ANSWER 19 OF 24 WPIDS (C) 2003 THOMSON DERWENT

AN 1999-357800 [30] WPIDS

DNC C1999-105876

TI Heteroaryl aminoguanidines and alkoxyguanidines and their solvates, hydrates or salts.

DC B03 B04 D22

IN LU, T; MARKOTAN, T P; SIEDEM, C; TOMCZUK, B E

PA (THRE-N) 3-DIMENSIONAL PHARM INC; (LUTT-I) LU T; (MARK-I) MARKOTAN T P; (SIED-I) SIEDEM C; (TOMC-I) TOMCZUK B E

CYC 85

PI WO 9926926 A1 19990603 (199930)* EN 145p

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL
OA PT SD SE SZ UG ZW

W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD
GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD
MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA
UG UZ VN YU ZW

AU 9917991 A 19990615 (199944)

US 6037356 A 20000314 (200020)

EP 1036063 A1 20000920 (200047) EN

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
RO SE SI

ZA 9810833 A 20000830 (200049) 143p

CN 1283189 A 20010207 (200129)

US 6245763 B1 20010612 (200135)

MX 2000005055 A1 20010201 (200168)

JP 2001524467 W 20011204 (200203) 203p

BR 9815325 A 20011226 (200206)

US 2002007070 A1 20020117 (200212)

US 6350764 B2 20020226 (200220)

US 2002086872 A1 20020704 (200247)

AU 751412 B 20020815 (200264)

US 6472399 B2 20021029 (200274)

ADT WO 9926926 A1 WO 1998-US25185 19981125; AU 9917991 A AU 1999-17991
19981125; US 6037356 A Provisional US 1997-66475P 19971126, Provisional US
1997-67324P 19971205, Provisional US 1998-79107P 19980323, US 1998-199167
19981125; EP 1036063 A1 EP 1998-962838 19981125, WO 1998-US25185 19981125;
ZA 9810833 A ZA 1998-10833 19981126; CN 1283189 A CN 1998-812495 19981125;
US 6245763 B1 Provisional US 1997-66475P 19971126, Provisional US
1997-67324P 19971205, Provisional US 1998-79107P 19980323, Div ex US
1998-199167 19981125, US 2000-482540 20000114; MX 2000005055 A1 MX
2000-5055 20000523; JP 2001524467 W WO 1998-US25185 19981125, JP
2000-522084 19981125; BR 9815325 A BR 1998-15325 19981125, WO 1998-US25185
19981125; US 2002007070 A1 Provisional US 1997-66475P 19971126,
Provisional US 1997-67324P 19971205, Provisional US 1998-79107P 19980323,
Div ex US 1998-199167 19981125, Div ex US 2000-482540 20000114, US
2001-827292 20010406; US 6350764 B2 Provisional US 1997-66475P 19971126,
Provisional US 1997-67324P 19971205, Provisional US 1998-79107P 19980323,
Div ex US 1998-199167 19981125, Div ex US 2000-482540 20000114, US

2001-827292 20010406; US 2002086872 A1 Provisional US 1997-66475P
19971126, Provisional US 1997-67324P 19971205, Provisional US 1998-79107P
19980323, Div ex US 1998-199167 19981125, Div ex US 2000-482540 20000114,
Div ex US 2001-827292 20010406, US 2001-12445 20011212; AU 751412 B AU
1999-17991 19981125; US 6472399 B2 Provisional US 1997-66475P 19971126,
Provisional US 1997-67324P 19971205, Provisional US 1998-79107P 19980323,
Div ex US 1998-199167 19981125, Div ex US 2000-482540 20000114, Div ex US
2001-827292 20010406, US 2001-12445 20011212

FDT AU 9917991 A Based on WO 9926926; EP 1036063 A1 Based on WO 9926926; US
6245763 B1 Div ex US 6037356; JP 2001524467 W Based on WO 9926926; BR
9815325 A Based on WO 9926926; US 2002007070 A1 Div ex US 6037356, Div ex
US 6245763; US 6350764 B2 Div ex US 6037356, Div ex US 6245763; AU 751412
B Previous Publ. AU 9917991, Based on WO 9926926; US 6472399 B2 Div ex US
6037356, Div ex US 6245763

PRAI US 1998-79107P 19980323; US 1997-66475P 19971126; US 1997-67324P
19971205; US 1998-199167 19981125; US 2000-482540 20000114; US
2001-827292 20010406; US 2001-12445 20011212

AB WO 9926926 A UPAB: 20021105

NOVELTY - Heteroaryl aminoguanidines and alkoxyguanidines are new.

DETAILED DESCRIPTION - Heteroaryl aminoguanidines and
alkoxyguanidines of formula (VII) and their solvates, hydrates or salts
are new:

R1 = alkyl, cycloalkyl, cycloalkylalkyl, alkenyl, alkynyl, aryl,
aralkyl, heterocycle or heterocycloalkyl (all optionally substituted);

Z' = SO₂, OCO, CO, NR₂CO or bond;

R2 = H, alkyl, aralkyl, aryl, 2-10C hydroxyalkyl, 2-10C aminoalkyl,
mono- or di-(2-10C) alkylamino or carboxyalkyl;

Het = a group of formula (i)-(iii);

R3-R5 = H, alkyl, cycloalkyl, alkenyl, alkynyl, optionally
substituted aryl, optionally aralkyl, optionally substituted heteroaryl,
trifluoromethyl, halo, hydroxyalkyl, cyano, nitro, carboxamido, CO₂R_x,
CH₂OR_x or OR_x;

R_x = H or alkyl or cycloalkyl (both with one or more unsaturations);

R6 = H, alkyl, aralkyl, aryl, cyano-(2-10C) alkyl, hydroxy-(2-10C)
alkyl, alkoxy-(2-10C) alkyl, mono- or di-alkylamino-(2-10C) alkyl or
carboxyalkyl;

R7 = H, 1-4C alkyl or 2-4C alkenyl;

R8 = H, alkyl, alkenyl, aralkyl, aryl, hydroxyalkyl, aminoalkyl,
mono- or di-alkylamino-(2-10C) alkyl or carboxyalkyl;

R12-R15 = H, alkyl, aralkyl, aryl, hydroxyalkyl, aminoalkyl, mono-
or di-alkylaminoalkyl or carboxyalkyl or, R12+R13 form (CH₂)_y, or R14+R15
form (CH₂)_q, or R12+R14 form (CH₂)_r;

y, q = 2-7;

r = 0-7;

X = O or NR₉;

R9 = H or alkyl, cycloalkyl or aryl (all optionally substituted by
amino, mono- or di-alkylamino, alkoxy, hydroxy, carboxy, alkoxycarbonyl,
aryloxycarbonyl, aralkoxycarbonyl, aryl, heteroaryl, acylamino, cyano or
trifluoromethyl);

Ra-Rc = H, alkyl, hydroxy, alkoxy, aryloxy, aralkoxy,
alkoxycarbonyloxy, cyano or CO₂R_w;

Rw = alkyl, cycloalkyl, phenyl, benzyl or a group of formula
(iv)-(v);

Rd-Rg = H, 1-6C alkyl, 2-6C alkenyl or phenyl;

Rh = aralkyl or 1-6C alkyl;

n = 0-8; and

m = 0-6.

ACTIVITY - Anti-pancreatitis; anti-thrombotic; anti-ischemic;
anti-stroke; anti-restenotic; anti-emphysema; anti-inflammatory.

MECHANISM OF ACTION - Trypsin-like protease inhibitor; proteolysis
inhibitor; thrombin inhibitor; platelet aggregation inhibitor; leukocyte
neutrophil elastase inhibitor; chymotrypsin inhibitor; pancreatic elastase
inhibitor; cathepsin G inhibitor; factor Xa inhibitor; thermolysin
inhibitor; metalloproteinase inhibitor; pepsin
inhibitor.

Assays based on the ability of test compound to inhibit the enzyme-catalyzed hydrolysis of peptide p-nitroanilide substrate were performed. Substrate was prepared in dimethylsulfoxide (DMSO) and diluted into assay buffer containing N-(2-hydroxyethyl)piperazine-N-2-ethanesulfonic acid (HEPES; 50 mM) and sodium chloride (200 mM) at pH 7.5. The final substrate concentration for trypsin was 4.3%. Test compounds were prepared as 1 mg/ml solutions in DMSO. Reactions were initiated by addition of 10 ml aliquot of enzyme and the absorbance increase at 405 nm was recorded for 15 minutes. Data corresponding to less than 10% hydrolysis were used in calculations. 3-Benzylsulfonylamino-6-methyl-1-((3-guanidinooxypropyl)aminocarbonylmethyl)-2-pyridinone trifluoroacetate (Ia) inhibited thrombin with a K_i value of 53 nM; (Ia) showed no inhibition of Factor Xa, chymotrypsin, elastase, plasmin or trypsin at 24 micro M.

USE - Used to inhibit proteolysis, trypsin-like protease, thrombin-induced platelet aggregation and clotting of fibrinogen in plasma (claimed). Used to treat pancreatitis, thrombosis, ischemia, stroke, restenosis, emphysema and inflammation (claimed). Used as a thrombin inhibitor in devices for blood collection, blood circulation and blood storage including catheters, blood dialysis machine, blood collection syringe or tube, blood lines or extracorporeal circuits or stents for surgical implantation into mammals (claimed). Also used to inhibit or treat aberrant proteolysis in mammals and to treat myocardial infarction, unstable angina, deep vein thrombosis, disseminated intravascular coagulation caused by trauma, sepsis or tumor metastasis, hemodialysis, cardiopulmonary bypass surgery, adult respiratory distress syndrome, endotoxic shock, rheumatoid arthritis, ulcerative colitis, induration, metastasis, hypercoagulability during chemotherapy, Alzheimer's disease, Down's syndrome, fibrin formation in the eye and wound healing as well as inflammatory responses, reperfusion damage, atherosclerosis, restenosis following balloon angioplasty, atherectomy and arterial stent placement and Parkinson's disease. Also used to reduce thrombogenicity of surfaces in mammals by attaching to the surface covalently or non-covalently, and for in vivo imaging of thrombi as diagnostic compositions.

ADVANTAGE - (I) are non-peptidic compounds that are potent and selective protease inhibitors with greater bioavailability and fewer side-effects than the prior art.

Dwg.0/0

L10 ANSWER 20 OF 24 WPIDS (C) 2003 THOMSON DERWENT
 AN 1998-362366 [31] WPIDS
 DNC C1998-111406
 TI New alpha-mercapto-amide peptide compounds - are matrix metallo-proteinase inhibitors, useful for treating diseases of tissue breakdown, e.g. bone resorption, inflammation, dermatological conditions, etc..
 DC B05
 IN FLOYD, C D
 PA (BRBI-N) BRITISH BIOTECH PHARM LTD
 CYC 37
 PI WO 9823588 A1 19980604 (199831)* EN 45p
 RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
 W: AU BR CA CN CZ GB HU IL JP KR MX NO NZ PL RU SG SK TR UA US
 AU 9851282 A 19980622 (199844)
 EP 944597 A1 19990929 (199945) EN
 R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU NL PT SE
 JP 2001509790 W 20010724 (200147) 46p
 ADT WO 9823588 A1 WO 1997-GB3258 19971127; AU 9851282 A AU 1998-51282 19971127; EP 944597 A1 EP 1997-945960 19971127, WO 1997-GB3258 19971127; JP 2001509790 W WO 1997-GB3258 19971127, JP 1998-524433 19971127
 FDT AU 9851282 A Based on WO 9823588; EP 944597 A1 Based on WO 9823588; JP 2001509790 W Based on WO 9823588
 PRAI GB 1996-24817 19961128
 AB WO 9823588 A UPAB: 19980805
 Alpha-mercaptoamide peptide compounds of formula (I) and their salts, hydrates and solvates are new: $R_2 = -(Alk)m-(Q)n-(Alk_1)p-Ar$; m, n, p =

0-1; Alk, Alk1 = divalent 1-3C alkylene; Q = O, S, SO or SO₂; Ar = optionally substituted phenyl or heteroaryl; R1 = H or acyl; R21 = (CH₂)_t-W; t = 1-4; W = 5-6-membered N-heterocyclic ring which (a) is attached via the N atom; (b) optionally contains N, O and/or S, SO or SO₂ as additional ring members; (c) is substituted by oxo on one or both of the C atoms adjacent to the linking N atom; and (d) is optionally benzo-fused or optionally substituted on one or more other C atoms by 1-6C alkyl, or oxo and/or on any additional N atoms by 1-6C alkyl, phenyl or heteroaryl; Z = 5-8-membered monocyclic or bridged N-heterocyclic ring that is attached by the N atom and that, when it is monocyclic, optionally contains as a ring member O, S, SO, SO₂ or NR₅; and/or is optionally substituted on one or more C atoms by OH, 1-6C alkyl, 1-6C alkoxy, cyano, oxo, ketalised oxo, amino, mono- or di-(1-6C) alkylamino, carboxy, 1-6C alkoxy-carbonyl, hydroxymethyl, 1-6C alkoxy-methyl, carbamoyl, mono- or di-(1-6C) alkyl-carbamoyl or hydroxyimino; or is a radical of formula (i): R₅ = H, OH, 1-6C alkyl, 1-6C alkoxy (1-6C) alkyl, benzyl, acyl, amino-protecting group or SO₂R₆; R₆ = 1-6C alkyl or optionally substituted phenyl or heteroaryl; R₃ = side-chain of (non)natural α-amino acid in which any functional groups may be protected; R₄ = optionally substituted phenyl, heteroaryl, cycloalkyl or cycloalkenyl, CHR_xR_y, -(Z'O)w-Z', 1-6C alkyl (which is optionally interrupted by one or more non-adjacent S and/or N atoms and is substituted by at least two (Z''')x-(OZ''')q groups), H, 1-6C alkyl, 1-4C perfluoroalkyl or D-(1-6C) alkyl; or R₃+R₄ = -C(Ra)(Rb)-A''-Alk₂-; R_{5a} = H or 1-6C alkyl; R_x, R_y = optionally substituted phenyl or heteroaryl ring optionally linked covalently to each other by a bond or by 1-4C alkylene or 2-4C alkenylene; or R_x = D1-(1-6C) alkyl-; and R_y = optionally substituted phenyl or heteroaryl; D1 = optionally substituted phenyl or heteroaryl; Z' = 1-6C alkyl optionally interrupted by one or more non-adjacent S and/or N atoms; w = integer >1, but no continuous linear sequence of atoms in R₄ is > 12; Z''' = 1-6C alkyl optionally interrupted by one or more non-adjacent S and/or N atoms; x = 0-1; q = 1-2, but no continuous linear sequence of atoms in R₄ is > 12; D = hydroxy, 1-6C alkoxy, 1-6C alkylthio, acylamino, optionally substituted phenyl or heteroaryl, NH₂ or mono- or di-(1-6C) alkylamino; Ra, Rb = H or 1-6C alkyl; A'' = bond, O, S, SS, NH or NR_{aa}; R_{aa} = 1-6C alkyl; Alk₂ = 1-6C alkylene.

USE - (I) are matrix metalloproteinase inhibitors, particularly metalloproteinases involved in tissue degradation. They may be useful in the treatment of diseases involving tissue breakdown, including bone resorption, inflammatory diseases, dermatological conditions, tumour growth and vascularisation, particularly rheumatoid arthritis, osteoarthritis, periodontitis, gingivitis, corneal ulceration and tumour invasion by secondary metastases.

Administration may be oral, parenteral or topical. Oral dosage units contain 1-250 (25-250) mg (I). Suitable daily dose is 0.1-300 (1-100) mg/kg/day. In eye treatment, dosage is e.g. 10-100 mg topically. For rheumatoid arthritis, administration may be oral or by intra-articular injection, using a daily dose of 10 mg - 1 g (for a 70 kg mammal).

ADVANTAGE - (I) have increased intrinsic activity and bioactivity as inhibitors of specific enzymes.

Dwg.0/0

L10 ANSWER 21 OF 24 WPIDS (C) 2003 THOMSON DERWENT

AN 1998-051838 [05] WPIDS

DNC C1998-017671

TI Treatment of pathological neovascularisation, e.g. ocular neovascular disease - using a combination of angiostatic compounds e.g. suramin, fumagillin, anti-mitotic and steroid.

DC B02 B05

IN CLARK, A F; DOSHI, R

PA (ALCO-N) ALCON LAB INC

CYC 21

PI WO 9741844 A1 19971113 (199805)* EN 53p

RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE

W: AU CA JP US

AU 9724382 A 19971126 (199813)
ADT WO 9741844 A1 WO 1997-US5574 19970403; AU 9724382 A AU 1997-24382 19970403
FDT AU 9724382 A Based on WO 9741844
PRAI US 1996-17096P 19960509
AB WO 9741844 A UPAB: 19980202

Method and composition for treating pathological neovascularisation in humans which comprises administration of a combination of two or more angiostatic compounds.

Angiostatic compound used are: anti-mitotics, estrogen metabolites, matrix **metalloproteinase inhibitors**, plasminogen activator/urokinase inhibitors, urokinase receptor antagonists, platelet factor 4 and analogues, heparinases, cartilage-derived inhibitor of angiogenesis, thrombospondin and related analogues, angiostatin, vasculostatin, proliferin-related protein, fumagillin-type compounds, tecogalan, pentosan polysulphate, thalidomide and related analogues, CM101, tyrosine kinase inhibitors, anti-sense oligonucleotides, suramin-type compound, angiostatic steroids, alpha v beta 3 and alpha v beta 5 integrin antagonists, cytotoxic antibodies against endothelial cell antigens, interferon, VEGF and bFGF antagonists, flk-1 and flt-1 antagonists, IL-1 and TFN antagonists.

USE - Used for treating and preventing **retinal** disease, rubeosis iritis, proliferative vitreo retinopathy inflammatory disease, chronic uveitis, neoplasm, Fuch's heterochromic iridocyclitis, neovascular glaucoma, corneal or optic nerve neovascularisation, vascular disease, pterygium, glaucoma surgery bleb failure, hyperkeratosis, cheloid formation and polyp formation.

ADVANTAGE - Combination therapy provides effective, multi-mechanistic angiostatic therapy which is more efficacious with fewer side effects.
Dwg.0/0

L10 ANSWER 22 OF 24 WPIDS (C) 2003 THOMSON DERWENT

AN 1996-151296 [15] WPIDS

DNC C1996-047504

TI New amino acid derivs. - useful as matrix **metalloprotease inhibitors**.

DC B03 B05 C02 C03 D21 E19

IN BECKETT, R P; MILLER, A; WHITTAKER, M

PA (BRBI-N) BRITISH BIOTECH PHARM LTD

CYC 33

PI WO 9606074 A1 19960229 (199615)* EN 58p

RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE

W: AU BR CA CN CZ DE FI GB HU JP KR NO NZ PL RU SK UA US

AU 9532622 A 19960314 (199625)

EP 777646 A1 19970611 (199728) EN

R: AT BE CH DE DK ES FR GB GR IE IT LI LU NL PT SE

JP 10504821 W 19980512 (199829) 54p

US 5763621 A 19980609 (199830)

EP 777646 B1 20010905 (200152) EN

R: AT BE CH DE DK ES FR GB GR IE IT LI LU NL PT SE

DE 69522569 E 20011011 (200168)

ADT WO 9606074 A1 WO 1995-GB1971 19950818; AU 9532622 A AU 1995-32622

19950818; EP 777646 A1 EP 1995-929157 19950818, WO 1995-GB1971 19950818;

JP 10504821 W WO 1995-GB1971 19950818, JP 1996-507870 19950818; US 5763621

A WO 1995-GB1971 19950818, US 1997-776693 19970220; EP 777646 B1 EP

1995-929157 19950818, WO 1995-GB1971 19950818; DE 69522569 E DE

1995-622569 19950818, EP 1995-929157 19950818, WO 1995-GB1971 19950818

FDT AU 9532622 A Based on WO 9606074; EP 777646 A1 Based on WO 9606074; JP

10504821 W Based on WO 9606074; US 5763621 A Based on WO 9606074; EP

777646 B1 Based on WO 9606074; DE 69522569 E Based on EP 777646, Based on

WO 9606074

PRAI GB 1994-16897 19940820

AB WO 9606074 A UPAB: 19960417

Aminoacid derivs. of formula (I) and their salts, hydrates and solvates are new: X = CO₂H or CONHOH; R₁ = H, 1-6C alkyl, 2=6C alkenyl, opt.

substd. phenyl, opt. substd. phenyl 1-6C alkyl, opt. substd. heterocyclyl

or opt. subst. heterocyclyl 1-6C alkyl; BSO_nA, opt. protected amino, acylamino, OH, SH, 1-6C alkoxy, 1-6C alkylamino, di 1-6C alkyl-amino, 1-6C alkylthio, aryl 1-6C alkyl, amino 1-6C alkyl, hydroxy 1-6C alkyl, mercapto 1-6C alkyl or carboxy 1-6C alkyl (where all amino, OH, SH or COOH gps. are opt. protected or COOH or amidated), lower alkyl subst. by carbamoyl, mono- or di lower alkylcarbamoyl, dilower alkylamino or carboxylower alkanoylamino; n = 0-2, B = H or 1-6C alkyl, Ph (opt. subst.), heterocyclyl, 1-6C acyl or opt. subst. phenacyl; A = 1-6C alkyl; R₂ = 1-6C alkyl, 2-6C alkenyl, 2-6C alkynyl, phenyl 1-6C alkyl, heteroaryl 1-6C alkyl, cycloalkyl 1-6C alkyl or cycloalkenyl (1-6C)alkyl (all opt. subst. by 1-6C alkyl, O(1-6C)alkyl, S(1-6C)alkyl, OPh, O(1-6Calkyl)Ph, halo or CN; R₃ = an alpha amino acid (opt. protected); R₄ = 3-8C cycloalkyl or 4-8C cycloalkenyl (both opt. subst.); R₅ = H or 1-6C alkyl.

USE - (I) are matrix **metalloprotease inhibitors** and TNF release inhibitors. They are used in human and veterinary medicine to treat or prevent diseases such as bone resorption disorders, inflammatory diseases, dermatological conditions and tumour invasion by secondary metastases, in partic. rheumatoid arthritis, osteoarthritis, periodontitis, gingivitis and corneal ulceration fever, cardiovascular disorders, haemorrhage, coagulation and acute phase response, cachexia and anorexia, acute infectins, shock, graft versus host reactions and autoimmune disease.

Dosage is 0.1-300 pref. 1-100 mg/kg/day P. O or 10-100 mg topically to the **eye**. Admin. is oral, topical or perenteral. For rheumatoid arthritis admin. is oral or i.a. at a dosage of 10mg-1g 1-10kg mammal.

ADVANTAGE - (I) are orally bioavailable.
Dwg.0/0

L10 ANSWER 23 OF 24 WPIDS (C) 2003 THOMSON DERWENT

AN 1994-358159 [44] WPIDS

DNC C1994-163420

TI New metallo- proteinase peptidyl derivs. - used to treat cancer, rheumatoid arthritis, osteoarthritis, multiple sclerosis, periodontal disease etc..

DC B05

IN MILLICAN, A T; MORPHY, R J

PA (CLLT) CELLTECH LTD; (CLLT) CELLTECH THERAPEUTICS LTD

CYC 2

PI WO 9425435 A1 19941110 (199444)* EN 40p

AU 9465754 A 19941121 (199508)

EP 648206 A1 19950419 (199520) EN

JP 08500610 W 19960123 (199642) 39p

ADT WO 9425435 A1 WO 1994-GB896 19940427; AU 9465754 A AU 1994-65754 19940427; EP 648206 A1 EP 1994-913710 19940427; WO 1994-GB896 19940427; JP 08500610 W JP 1994-524027 19940427, WO 1994-GB896 19940427

FDT AU 9465754 A Based on WO 9425435; EP 648206 A1 Based on WO 9425435; JP 08500610 W Based on WO 9425435

PRAI GB 1993-8695 19930427

AB WO 9425435 A UPAB: 19950721

Peptidyl derivs. of formula (I) and their salts, solvates, hydrates and prodrugs are new. R = CONHOR₆, opt. esterified carboxy, SR₆ or P(O)(X₁R₇)X₂R₈; R₆ = H or acyl; X₁, X₂ = O or S; R₇, R₈ = H or opt. subst. alkyl, aryl or aralkyl; R₁ = H or opt. subst. alkyl, alkenyl, aryl, aralkyl, heteroaralkyl or heteroarylthioalkyl; R₂ = opt. subst. alkyl, alkenyl, cycloalkyl, cycloalkylalkyl, aryl, opt. subst. amino or opt. esterified carboxy; R₃ = H or alkyl; R₄ = H or alkyl; R₅ = CR₉R₁₀HetR₁₁; R₉, R₁₀ = opt. subst. alkyl or alkenyl opt. interrupted by O, S and/or N(R₁₂) or opt. subst. cycloalkyl, cycloalkenyl, aryl or heteroaryl; or CR₉R₁₀ = 3-6C cycloalkyl or cycloalkenyl; Het = O, S(O)p or N(R₁₂); p = 0-2; R₁₁ = H, aliphatic, cycloaliphatic, heterocycloaliphatic, aromatic or heteroaromatic gp.; X = opt. subst. amino or OH; or X+Het = X'-Alk'R₅'; X' = N(R₁₂); Alk' = opt. subst. alkylene; and R₅' = Het-C(R₉)(R₁₀).

USE - (I) are **metalloproteinase inhibitors** with good duration of action. They are used to treat or prevent diseases or

disorders in which stromelysin, collagenase and gelatin are involved e.g. to treat cancer to control the development of tumour metastases. They are used to treat or prevent musculo-skeletal disorders, e.g. arthritic disease such as rheumatoid arthritis, osteoarthritis and septic arthritis and to prevent tumour cell metastasis and invasion. They are partic. used to treat cancer pref. in conjunction with radiotherapy, chemotherapy or surgery or in patients with primary tumours to control development of tumour metastasis. Particular cancers include breast, melanoma, lung, head, neck or bladder cancers. The cpds. may also be used to prevent myelin degradation in the CNS and peripheral nervous system e.g. for treating multiple sclerosis, for controlling periodontal diseases such as gingivitis and for use in tissue remodelling. They may also be used to treat or prevent angiogenic disease, e.g. characterised by pathological growth or new capillaries, esp. solid tumours and arthritis diseases as above, psoriasis, eye diseases such as proliferative retinopathies, neovascular glaucoma and ocular tumours, angiofibromas and hemangiomas.

ADVANTAGE - (I) have good oral bioavailability and after oral admin. have longer duration of action than related known cpds. such as those of WO9209564-A.

Dwg.0/0

L10 ANSWER 24 OF 24 WPIDS (C) 2003 THOMSON DERWENT
 AN 1993-242869 [30] WPIDS
 CR 1992-192222 [23]; 1992-216967 [26]; 1992-216973 [26]; 1993-404979 [50];
 1994-332697 [41]; 1995-275232 [36]
 DNC C1993-108182
 TI Inhibition of angiogenesis - by contacting tissue with mammalian matrix
 metallo-protease inhibitor, for treating e.g. cancer and immune system
 disorders.
 DC B05
 IN GALARDY, R E
 PA (GLYC-N) GLYCOMED INC; (GALA-I) GALARDY R E
 CYC 22
 PI WO 9313741 A2 19930722 (199330)* EN 52p
 RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
 W: AU CA DK JP NO
 AU 9334332 A 19930803 (199348)
 US 5268384 A 19931207 (199350) 14p
 WO 9313741 A3 19930819 (199513)
 JP 07503007 W 19950330 (199521)
 EP 663823 A1 19950726 (199534) EN
 R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
 EP 663823 A4 19970604 (199746)
 US 5696147 A 19971209 (199804) 15p
 EP 663823 B1 20001122 (200061) EN
 R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
 DE 69329699 E 20001228 (200107)
 ADT WO 9313741 A2 WO 1993-US54 19930104; AU 9334332 A AU 1993-34332 19930104,
 WO 1993-US54 19930104; US 5268384 A CIP of US 1990-615798 19901121, CIP of
 US 1991-747751 19910820, CIP of US 1991-747752 19910820, US 1992-817039
 19920107; JP 07503007 W JP 1993-512526 19930104, WO 1993-US54 19930104; EP
 663823 A1 EP 1993-902938 19930104, WO 1993-US54 19930104; EP 663823 A4 EP
 1993-902938 ; US 5696147 A CIP of US 1990-615798 19901121, CIP of
 US 1991-747751 19910820, CIP of US 1991-747752 19910820, Cont of US
 1992-817039 19920107, US 1993-161786 19931203; EP 663823 B1 EP 1993-902938
 19930104, WO 1993-US54 19930104; DE 69329699 E DE 1993-629699 19930104, EP
 1993-902938 19930104, WO 1993-US54 19930104
 FDT AU 9334332 A Based on WO 9313741; US 5268384 A CIP of US 5183900, CIP of
 US 5189178, CIP of US 5239078; JP 07503007 W Based on WO 9313741; EP
 663823 A1 Based on WO 9313741; US 5696147 A CIP of US 5183900, CIP of US
 5189178, CIP of US 5239078, Cont of US 5268384; EP 663823 B1 Based on WO
 9313741; DE 69329699 E Based on EP 663823, Based on WO 9313741
 PRAI US 1992-817039 19920107; US 1990-615798 19901121; US 1991-747751
 19910820; US 1991-747752 19910820; US 1993-161786 19931203

AB WO 9313741 A UPAB: 20010202

Inhibition of angiogenesis comprises contacting a tissue (in which angiogenesis is taking place) with a synthetic mammalian matrix metalloprotease inhibitor (I).

Pref. (I), is $QCH_2CH(i-Bn)CONHCHR'4COOH$, $YQ'CON(R3)CHR4COX$ or $R7ONR6COQ'CON(R3)CHR4COX$, $Q = HONHCONH$ or $ROOC$; $Q1 = (CHR1)nCHR2$ or $(CHR1)m-C(R1)=C(R2)$; $R = H$ or 1-6C alkyl; $R4' = (3-indolyl)$ methylene; each $R1 = H$ or 1-8C alkyl; each $R2 = H$ or 1-8C alkyl; or $R1 + R2 = (CH_2)p$; $p = 3-5$; $R3 = H$ or 1-4C alkyl; $R4 =$ fused or conjugated bicycloaryl methylene (opt. substd); $n = 0, 1$ or 2 ; $m = 0$ or 1 ; $X = OR_5, NHR_5$, a cyclic amine or heterocyclic amine residue, or an amino acid residue (or corresp. amide); $R_5 = H$ or opt. substd. 1-12C alkyl, 6-12C aryl or 6-16C aryl-alkyl; $R_6 = H$ or 1-4C alkyl; $R_7 = H$, 1-4C alkyl or acyl; $Y = H$, 1-4C alkyl or acyl; $Y = R7ONR6CONR_6, (R_6)2NCONOR_7$ or $R6CONOR_7$; The $CONR_3$ gp. is opt. replaced by $CH_2NR_3, CH_2CHR_3, CH=CR_3, COCHR_3, CH(OH)CHR_3, NR_3CO$ or $CF=CR_3$.

USE/ADVANTAGE - The method can be used to treat cancer (including angiosarcoma, kaposi's sarcoma, glioblastoma multiforme, hemangioblastoma, Hippel-Lindau disease and Lemangiopericytoma), eye conditions such as neovascular glaucoma and diabetic retinopathy, immune system disorders (such as rheumatoid arthritis or angiolymphoid hyperplasia), or skin conditions (such as cavernous hemangioma or psoriasis). Admin. is by injection, orally or topically. Injected doses are 0.1 micro mg/kg to 1 mg/kg
Dwg.0/0

=> file uspatful

COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
96.36	133.50

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE	TOTAL
ENTRY	SESSION
0.00	-5.58

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FILE 'USPATFULL' ENTERED AT 14:47:52 ON 12 FEB 2003

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FILE COVERS 1971 TO PATENT PUBLICATION DATE: 11 Feb 2003 (20030211/PD)

FILE LAST UPDATED: 11 Feb 2003 (20030211/ED)

HIGHEST GRANTED PATENT NUMBER: US6519773

HIGHEST APPLICATION PUBLICATION NUMBER: US2003028945

CA INDEXING IS CURRENT THROUGH 11 Feb 2003 (20030211/UPCA)

ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 11 Feb 2003 (20030211/PD)

REVISED CLASS FIELDS (/NCL) LAST RELOADED: Dec 2002

USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Dec 2002

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>>> applications. USPAT2 contains full text of the latest US <<<
>>> publications, starting in 2001, for the inventions covered in <<<
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>>> /PK, etc. <<<
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>>> enter this cluster. <<<
>>> <<<
>>> Use USPATALL when searching terms such as patent assignees, <<<
```

>>> classifications, or claims, that may potentially change from <<<
>>> the earliest to the latest publication. <<<

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substance identification.

=> s 130370-60-4/rn
L11 30 130370-60-4/RN

=> s batimastat
L12 159 BATIMASTAT

=> s l11 or l12
L13 172 L11 OR L12

=> s eye or retina
134855 EYE
49960 EYES
160314 EYE
(EYE OR EYES)
8438 RETINA
844 RETINAS
113 RETINAE
8733 RETINA
(RETINA OR RETINAS OR RETINAE)
L14 162347 EYE OR RETINA

=> s l13 and l14
L15 62 L13 AND L14

=> s topical
45918 TOPICAL
102 TOPICALS
L16 45932 TOPICAL
(TOPICAL OR TOPICALS)

=> s l15 and l16
L17 48 L15 AND L16

=> d ti l15 1-10

L15 ANSWER 1 OF 62 USPATFULL
TI Methods for enhancing antibody-induced cell lysis and treating cancer

L15 ANSWER 2 OF 62 USPATFULL
TI Particles with improved solubilization capacity

L15 ANSWER 3 OF 62 USPATFULL
TI Novel functional agents for magnetic resonance imaging

L15 ANSWER 4 OF 62 USPATFULL
TI Purposeful movement of human migratory cells away from an agent source

L15 ANSWER 5 OF 62 USPATFULL
TI 3-heterocyclylpropanohydroxamic acid PCP inhibitors

L15 ANSWER 6 OF 62 USPATFULL
TI Aromatic sulfone hydroxamic acid metalloprotease inhibitor

L15 ANSWER 7 OF 62 USPATFULL
TI Aromatic sulfonyl alpha-hydroxy hydroxamic acid compounds

L15 ANSWER 8 OF 62 USPATFULL
TI Use of neomycin for treating angiogenesis-related diseases

L15 ANSWER 9 OF 62 USPATFULL
 TI Methods and products related to low molecular weight heparin

L15 ANSWER 10 OF 62 USPATFULL
 TI Medical use of matrix metalloproteinase inhibitors for inhibiting tissue contraction

=> d ti l15 11-62

L15 ANSWER 11 OF 62 USPATFULL
 TI N-hydroxy 4-sulfonyl butanamide compounds

L15 ANSWER 12 OF 62 USPATFULL
 TI Immunostimulatory nucleic acids and cancer medicament combination therapy for the treatment of cancer

L15 ANSWER 13 OF 62 USPATFULL
 TI 3-ox(adi) azolylpropanohydroxamic acids useful as procollagen C-Proteinase inhibitors

L15 ANSWER 14 OF 62 USPATFULL
 TI CaR receptor as a mediator of migratory cell chemotaxis and/or chemokinesis

L15 ANSWER 15 OF 62 USPATFULL
 TI Pore structures for reduced pressure aerosolization

L15 ANSWER 16 OF 62 USPATFULL
 TI Amidoaromatic ring sulfonamide hydroxamic acid compounds

L15 ANSWER 17 OF 62 USPATFULL
 TI Compositions and methods for the treatment of cancer

L15 ANSWER 18 OF 62 USPATFULL
 TI Methods and products related to pulmonary delivery of polysaccharides

L15 ANSWER 19 OF 62 USPATFULL
 TI Purposeful movement of human migratory cells away from an agent source

L15 ANSWER 20 OF 62 USPATFULL
 TI Heparinase III and uses thereof

L15 ANSWER 21 OF 62 USPATFULL
 TI Sulfonyl divalent aryl or heteroaryl hydroxamic acid compounds

L15 ANSWER 22 OF 62 USPATFULL
 TI Diagnostics and therapeutics for ocular disorders

L15 ANSWER 23 OF 62 USPATFULL
 TI Solvent systems for pharmaceutical agents

L15 ANSWER 24 OF 62 USPATFULL
 TI Ocular treatment device

L15 ANSWER 25 OF 62 USPATFULL
 TI Inhibition of invasive remodelling

L15 ANSWER 26 OF 62 USPATFULL
 TI N-carboxymethyl substituted benzolactams as inhibitors of matrix metalloproteinase

L15 ANSWER 27 OF 62 USPATFULL
 TI Pore structures for reduced pressure aerosolization

L15 ANSWER 28 OF 62 USPATFULL
 TI ISOLATED NUCLEIC ACID MOLECULES ENCODING HUMAN PROTEASE PROTEINS, AND
 USES THEREOF

L15 ANSWER 29 OF 62 USPATFULL
 TI Methods of ophthalmic administration

L15 ANSWER 30 OF 62 USPATFULL
 TI Cosmetic composition and method

L15 ANSWER 31 OF 62 USPATFULL
 TI Medical use of matrix metalloproteinase inhibitors for inhibiting tissue
 contraction

L15 ANSWER 32 OF 62 USPATFULL
 TI Methods of ophthalmic administration

L15 ANSWER 33 OF 62 USPATFULL
 TI Combinations and methods for treating neoplasms

L15 ANSWER 34 OF 62 USPATFULL
 TI Method of using matrix metalloproteinase inhibitors in filtering blebs
 following glaucoma filtering surgery and in the treatment of ischemic
 damage to the retina and optic nerve

L15 ANSWER 35 OF 62 USPATFULL
 TI 3-substituted pyrrolidines useful as inhibitors of matrix
 metalloproteinases

L15 ANSWER 36 OF 62 USPATFULL
 TI Aromatic sulfonyl alpha-hydroxy hydroxamic acid compounds

L15 ANSWER 37 OF 62 USPATFULL
 TI Compositions and methods for the treatment of cancer

L15 ANSWER 38 OF 62 USPATFULL
 TI Pore structures for reduced pressure aerosolization

L15 ANSWER 39 OF 62 USPATFULL
 TI Combination therapy

L15 ANSWER 40 OF 62 USPATFULL
 TI Matrix metalloprotease inhibitors

L15 ANSWER 41 OF 62 USPATFULL
 TI Use of certain drugs for treating nerve root injury

L15 ANSWER 42 OF 62 USPATFULL
 TI Amidomalonamides useful as inhibitors of MMP of matrix metalloproteinase

L15 ANSWER 43 OF 62 USPATFULL
 TI Immunostimulatory nucleic acids for inducing a Th2 immune response

L15 ANSWER 44 OF 62 USPATFULL
 TI AROMATIC SULFONE HYDROXAMIC ACID METALLOPROTEASE INHIBITOR

L15 ANSWER 45 OF 62 USPATFULL
 TI Procollagen C-proteinase inhibitors

L15 ANSWER 46 OF 62 USPATFULL
 TI SULFONYL DIVALENT ARYL OR HETEROARYL HYDROXAMIC ACID COMPOUNDS

L15 ANSWER 47 OF 62 USPATFULL
 TI AROMATIC SULFONE HYDROXAMIC ACID METALLOPROTEASE INHIBITOR

L15 ANSWER 48 OF 62 USPATFULL
 TI Aerosol-forming porous membrane with certain pore structure

L15 ANSWER 49 OF 62 USPATFULL
 TI Attaching agents to tissue with transglutaminase and a transglutaminase substrate

L15 ANSWER 50 OF 62 USPATFULL
 TI 3-(thio-substitutedamido)-lactams useful as inhibitors of matrix metalloproteinase

L15 ANSWER 51 OF 62 USPATFULL
 TI Method and device for creating aerosol with porous membrane with certain pore structure

L15 ANSWER 52 OF 62 USPATFULL
 TI Alkenyl- and alkynyl-containing metalloprotease inhibitors

L15 ANSWER 53 OF 62 USPATFULL
 TI Medical use of matrix metalloproteinase inhibitors for inhibiting tissue contraction

L15 ANSWER 54 OF 62 USPATFULL
 TI Thioaryl sulfonamide hydroxamic acid compounds

L15 ANSWER 55 OF 62 USPATFULL
 TI Aerosol-forming porous membrane with certain pore structure

L15 ANSWER 56 OF 62 USPATFULL
 TI Encoder and decoder

L15 ANSWER 57 OF 62 USPATFULL
 TI Polynucleotides encoding urogenital sinus derived growth inhibitory factor and vectors

L15 ANSWER 58 OF 62 USPATFULL
 TI Prefilter for prevention of clogging of a nozzle in the generation of an aerosol and prevention of administration of undesirable particles

L15 ANSWER 59 OF 62 USPATFULL
 TI Inhibition of TNF production with matrix metalloproteinase inhibitors

L15 ANSWER 60 OF 62 USPATFULL
 TI Hydroxamic acid based collagenase inhibitors

L15 ANSWER 61 OF 62 USPATFULL
 TI Hydroxamino acid based collagenase inhibitors

L15 ANSWER 62 OF 62 USPATFULL
 TI Hydroxamic acid based collagenase inhibitors

=> d bib ab 22 23 24 30 29 32 34 37 39 41 52 53 59
 48 ANSWERS ARE AVAILABLE. SPECIFIED ANSWER NUMBER EXCEEDS ANSWER SET SIZE
 The answer numbers requested are not in the answer set.
 ENTER ANSWER NUMBER OR RANGE (1):end

=> d bib ab 22 23 24 30 29 32 34 37 39 41 52 53 59 115

L15 ANSWER 22 OF 62 USPATFULL
 AN 2002:191516 USPATFULL
 TI Diagnostics and therapeutics for ocular disorders
 IN Hageman, Gregory S., Coralville, IA, UNITED STATES
 Mullins, Robert F., Coralville, IA, UNITED STATES
 PI US 2002102581 A1 20020801

AI US 2001-949261 A1 20010906 (9)
RLI Continuation-in-part of Ser. No. US 2000-510230, filed on 22 Feb 2000,
PENDING Continuation-in-part of Ser. No. US 2001-845745, filed on 30 Apr
2001, PENDING
PRAI US 1999-120822P 19990219 (60)
US 1999-120668P 19990219 (60)
US 1999-123052P 19990305 (60)
US 2000-200698P 20000429 (60)
DT Utility
FS APPLICATION
LREP TOWNSEND AND TOWNSEND AND CREW, LLP, TWO EMBARCADERO CENTER, EIGHTH
FLOOR, SAN FRANCISCO, CA, 94111-3834
CLMN Number of Claims: 24
ECL Exemplary Claim: 1
DRWN 1 Drawing Page(s)
LN.CNT 5644
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention relates to methods for treating, preventing and diagnosing
drusen-associated disorders.

L15 ANSWER 23 OF 62 USPATFULL
AN 2002:191217 USPATFULL
TI Solvent systems for pharmaceutical agents
IN Anderson, David M., Colonial Heights, VA, UNITED STATES
PI US 2002102280 A1 20020801
AI US 2001-994937 A1 20011128 (9)
PRAI US 2000-253874P 20001129 (60)
DT Utility
FS APPLICATION
LREP Whitham, Curtis & Christofferson, PC, 11491 Sunset Hills Road - #430,
Reston, VA, 20190
CLMN Number of Claims: 56
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2361
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention provides compositions, solvent systems, and methods for
solubilizing compounds which are otherwise difficult to solubilize. The
invention involves the use of a structured fluid (e.g. a liquid
crystalline phase, an L1 phase, an L2 phase, an L3 phase, an emulsion,
or a microemulsion), comprising a polar solvent, a lipid or a
surfactant, and an essential oil or a dissolution/solubilization agent.

L15 ANSWER 24 OF 62 USPATFULL
AN 2002:187971 USPATFULL
TI Ocular treatment device
IN Embleton, Jonathan K., Newbury, UNITED KINGDOM
Jones, Stephen P., Glasgow, UNITED KINGDOM
Malcolmson, Richard J., Swindon, UNITED KINGDOM
Martini, Luigi G., Birkenhead, UNITED KINGDOM
Houzeo, Peter J., Oakington, UNITED KINGDOM
Rocca, Sarah A., Girton, UNITED KINGDOM
Stevens, Howard N., Glasgow, UNITED KINGDOM
PA R. P. Scherer Corporation, Troy, MI, United States (U.S. corporation)
PI ~~US 6425888~~ B1 20020730
WO 9606581 19960307
AI US 1997-793299 19970811 (8)
WO 1995-GB2040 19950830
19970811 PCT 371 date
PRAI GB 1994-17399 19940830
DT Utility
FS GRANTED
EXNAM Primary Examiner: McDermott, Corrine; Assistant Examiner: Cho, David J.
LREP McDonnell Boehnen Hulbert & Berghoff, Sarussi, Steven J.
CLMN Number of Claims: 22

ECL Exemplary Claim: 1
DRWN 21 Drawing Figure(s); 8 Drawing Page(s)
LN.CNT 803

AB A unit container for a treatment fluid comprises a sealed enclosure of which one wall section thereof is formed with at least one opening. The enclosure is pressuriseable to discharge its contents through the opening or openings, which is or are of sufficient diameter to enable the generation of a jet and/or discrete droplets of treatment fluid discharged therefrom. The one wall section is typically a flat section of the enclosure wall, and the enclosure is typically a blister pack, with the wall section at a planar base of the blister. However, the one wall section may be dome-shaped and formed with at least one opening in the top region of the dome. Containers of the invention may be provided in packages, for example in strip form or in planar arrays. Dispensing devices are described for discharging their contents in treatment.

L15 ANSWER 30 OF 62 USPATFULL

AN 2002:105720 USPATFULL

TI Cosmetic composition and method

IN Lerner, David S., Boca Raton, FL, UNITED STATES
Schultz, Gregory, Gainesville, FL, UNITED STATES

PI US 2002054922 A1 20020509

AI US 2001-896566 A1 20010629 (9)

PRAI US 2000-215087P 20000629 (60)

DT Utility

FS APPLICATION

LREP Timothy H. Van Dyke, Bencen & Van Dyke, P.A., 1630 Hillcrest Street,
Orlando, FL, 32803

CLMN Number of Claims: 23

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 421

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The cosmetic topical formulation of this invention is directed toward diminishing skin wrinkling, fine line, improving skin tone, and combinations thereof. Preferably, the topical formulation contains a matrix metalloproteinase inhibitor, MMPI, and advantageously includes a natural estrogen, e.g., a true estrogen compound, such as 17-beta estradiol, or an estrogen-like steroid, (such as various phytoestrogens found in herbal preparations), as opposed to a synthetic estrogen. Other forms of the cosmetic topical formulation of this invention include combinations of synthetic estrogen and MMP inhibitor. Exemplary synthetic estrogens include, but are not limited to, ethinyl estradiol and clomiphene citrate. The cosmetic topical formulation is safe and effective diminishing wrinkling, and improving skin tone. Certain compositions of this invention are useful for minimizing photodamage to skin, while in other embodiments, the composition according to this invention is useful to prevent or minimize the adverse effects on skin induced by cigarette smoking.

L15 ANSWER 29 OF 62 USPATFULL

AN 2002:128474 USPATFULL

TI Methods of ophthalmic administration

IN Bowman, Lyle M., Pleasanton, CA, United States
Pfeiffer, James F., Oakland, CA, United States
Clark, Leslie A., Alameda, CA, United States
Hecker, Karl I., Keene, NH, United States

PA InSite Vision Incorporated, Alameda, CA, United States (U.S.
corporation)

PI US 6397849 B1 20020604

AI US 1999-366072 19990802 (9)

RLI Continuation-in-part of Ser. No. US 1998-127920, filed on 3 Aug 1998

DT Utility

FS GRANTED

EXNAM Primary Examiner: Willse, David H.; Assistant Examiner: Barrett, Thomas

LREP Arnold & Porter
CLMN Number of Claims: 60
ECL Exemplary Claim: 1
DRWN 1 Drawing Figure(s); 1 Drawing Page(s)
LN.CNT 1090
AB Intrasccleral injection of a therapeutic or diagnostic material at a location overlying the **retina** provides a minimally invasive technique for delivering the agent to the posterior segment of the **eye**. The procedure also allows for close proximity of the material to the targeted site and can be effectively used to treat conditions associated with the posterior segment of the **eye**, including macular degeneration, vein occlusion, and diabetic retinopathy. The sclera can be used to hold a depot of the material such as for sustained released or as a conduit for propelling material through whereby the material is delivered immediately to the underlying tissues but without physically penetrating the sclera with an instrument or otherwise unreasonably traumatizing the **eye**.

L15 ANSWER 32 OF 62 USPATFULL

AN 2002:94339 USPATFULL
TI Methods of ophthalmic administration
IN Bowman, Lyle M., Pleasanton, CA, United States
Pfeiffer, James F., Oakland, CA, United States
Clark, Leslie A., Alameda, CA, United States
Hecker, Karl L., Keene, NH, United States
PA InSite Vision, Incorporated, Alameda, CA, United States (U.S. corporation)
PI US 6378526 B1 20020430
AI US 1998-127920 19980803 (9)
DT Utility
FS GRANTED
EXNAM Primary Examiner: McDermott, Corrine; Assistant Examiner: Barrett, Thomas C.

LREP Arnold & Porter
CLMN Number of Claims: 29
ECL Exemplary Claim: 1
DRWN 1 Drawing Figure(s); 1 Drawing Page(s)
LN.CNT 823

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Intrasccleral injection of a therapeutic or diagnostic material at a location overlying the **retina** provides a minimally invasive technique for delivering the agent to the posterior segment of the **eye**. The procedure also allows for close proximity of the material to the targeted site and can be effectively used to treat conditions associated with the posterior segment of the **eye**, including macular degeneration, vein occlusion, and diabetic retinopathy.

L15 ANSWER 34 OF 62 USPATFULL

AN 2002:78745 USPATFULL
TI Method of using matrix metalloproteinase inhibitors in filtering blebs following glaucoma filtering surgery and in the treatment of ischemic damage to the **retina** and optic nerve
IN Schuman, Joel S., Wayland, MA, UNITED STATES
Fini, M. Elizabeth, Milton, MA, UNITED STATES
Chintala, Shravan K., Quincy, MA, UNITED STATES
PI US-2002042402 A1 20020411
US 6503892 B2 20030107
AI US 2001-841936 A1 20010425 (9)
PRAI US 2000-199881P 20000426 (60)
DT Utility
FS APPLICATION
LREP Ivor R. Elrifi Esq., Mintz, Levin, Cohn, Ferris,, Glovsky and Popeo P. C., One Financial Center, Boston, MA, 02111
CLMN Number of Claims: 47

ECL Exemplary Claim: 1
DRWN 8 Drawing Page(s)
LN.CNT 1120

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention provides a method of inhibiting, preventing, and/or treating conjunctival filtering bleb leaks that may occur following glaucoma filtering surgery by administering Matrix Metalloproteinase inhibitors to glaucoma patients who have undergone such surgery. The invention additionally includes a method of using Matrix Metalloproteinase inhibitors to inhibit, prevent, and/or treat ischemic damage to the retina and optic nerve in patients in need of such treatment.

L15 ANSWER 37 OF 62 USPATFULL

AN 2002:61254 USPATFULL

TI Compositions and methods for the treatment of cancer

IN Zeldis, Jerome B., Princeton, NJ, UNITED STATES

Zeitlin, Andrew L., Basking Ridge, NJ, UNITED STATES

Barer, Sol, Westfield, NJ, UNITED STATES

PI US 2002035090 A1 20020321

AI US 2001-853617 A1 20010514 (9)

PRAI US 2000-204143P 20000515 (60)

DT Utility

FS APPLICATION

LREP PENNIE & EDMONDS LLP, 1667 K STREET NW, SUITE 1000, WASHINGTON, DC, 20006

CLMN Number of Claims: 60

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 1973

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention relates to compositions comprising thalidomide and another anti-cancer drug which can be used in the treatment or prevention of cancer. Preferred anti-cancer drugs are topoisomerase inhibitors. A particular composition comprises thalidomide, or a pharmaceutically acceptable salt, solvate, or clathrate thereof, and irinotecan. The invention also relates to methods of treating or preventing cancer which comprise the administration of a thalidomide and another anti-cancer drug to a patient in need of such treatment or prevention. The invention further relates to methods of reducing or avoiding adverse side effects associated with the administration of chemotherapy or radiation therapy which comprise the administration of thalidomide to a patient in need of such reduction or avoidance.

L15 ANSWER 39 OF 62 USPATFULL

AN 2002:43558 USPATFULL

TI Combination therapy

IN Wood, Lars Michael, Oxford, UNITED KINGDOM

Laber, David Olum, Oxford, UNITED KINGDOM

Wright, Annette, Oxford, UNITED KINGDOM

PI US 2002025925 A1 20020228

AI US 2001-851328 A1 20010509 (9)

RLI Continuation of Ser. No. US 1999-254418, filed on 8 Mar 1999, ABANDONED

PRAI GB 1996-19631 19960920

DT Utility

FS APPLICATION

LREP BANNER & WITCOFF, 1001 G STREET N W, SUITE 1100, WASHINGTON, DC, 20001

CLMN Number of Claims: 10

ECL Exemplary Claim: 1

DRWN 8 Drawing Page(s)

LN.CNT 887

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates to the use of a matrix metalloproteinase inhibitor and a cyclosporin in combination therapy for treating mammals suffering from arthritic diseases such as rheumatoid arthritis.

L15 ANSWER 41 OF 62 USPATFULL
 AN 2001:237482 USPATFULL
 TI Use of certain drugs for treating nerve root injury
 IN Olmarker, Kjell, Molndal, Sweden
 Rydevik, Bjorn, Goteborg, Sweden
 PI US 2001055594 A1 20011227
 AI US 2001-826893 A1 20010406 (9)
 RLI Continuation-in-part of Ser. No. US 2001-743852, filed on 17 Jan 2001,
 PENDING A 371 of International Ser. No. WO 1999-SE1671, filed on 23 Sep
 1999, UNKNOWN
 PRAI SE 1998-3276 19980925
 SE 1998-3710 19981029
 DT Utility
 FS APPLICATION
 LREP Benton S. Duffett, Jr., BURNS, DOANE, SWECKER & MATHIS, L.L.P., P.O. Box
 1404, Alexandria, VA, 22313-1404
 CLMN Number of Claims: 29
 ECL Exemplary Claim: 1
 DRWN No Drawings
 LN.CNT 1211
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.
 AB The present invention relates to pharmaceutical compositions for the
 treatment of spinal disorders caused by the liberation of TNF-.alpha.
 comprising an effective amount of a TNF-.alpha. inhibitor, as well as a
 method for treatment of such disorders, and the use of TNF-.alpha.
 inhibitors in the preparation of pharmaceutical compositions for such
 treatment.

L15 ANSWER 52 OF 62 USPATFULL
 AN 2001:33267 USPATFULL
 TI Alkenyl- and alkynl-containing metalloprotease inhibitors
 IN Natchus, Michael George, Glendale, OH, United States
 Bookland, Roger Gunnard, Cincinnati, OH, United States
 Almstead, Neil Gregory, Loveland, OH, United States
 Pikul, Stanislaw, Mason, OH, United States
 De, Biswanath, Cincinnati, OH, United States
 Cheng, Menyan, West Chester, OH, United States
 PA The Procter & Gamble Co., Cincinnati, OH, United States (U.S.
 corporation)
 PI US 6197770 B1 20010306
 AI US 2000-517080 20000301 (9)
 PRAI US 1999-122644P 19990303 (60)
 DT Utility
 FS Granted
 EXNAM Primary Examiner: Ramsuer, Robert W.
 LREP Roof, Carl J., Clark, Karen F.
 CLMN Number of Claims: 45
 ECL Exemplary Claim: 1
 DRWN No Drawings
 LN.CNT 4321
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.
 AB Disclosed are compounds which are inhibitors of metalloproteases and
 which are effective in treating conditions characterized by excess
 activity of these enzymes. In particular, the compounds have a structure
 according to the following Formula (I): ##STR1##

where X, W, Z, A, G, R.sup.1, R.sup.2, R.sup.3, R.sup.4, R.sup.5,
 R.sup.5' and k have the meanings described in the specification. This
 invention also includes optical isomers, diastereomers and enantiomers
 of the formula above, and pharmaceutically-acceptable salts,
 biohydrolyzable amides, esters, and imides thereof Also described are
 pharmaceutical compositions comprising these compounds, and methods of
 treating or preventing metalloprotease-related maladies using the
 compounds or the pharmaceutical compositions.

L15 ANSWER 53 OF 62 USPATFULL
 AN 2000:94697 USPATFULL
 TI Medical use of matrix metalloproteinase inhibitors for inhibiting tissue contraction
 IN Khaw, Peng Tee, London, United Kingdom
 Schultz, Gregory S., Gainesville, FL, United States
 PA University of Florida Research Found, Gainesville, FL, United States
 (U.S. corporation)
 Institute of Ophthalmology, London, United Kingdom (non-U.S. corporation)
 Moorfields Eye Hospital NHS Trust, London, United Kingdom (non-U.S. corporation)
 PI US 6093398 20000725
 WO 9524921 19950921
 AI US 1996-716155 19961119 (8)
 WO 1995-GB576 19950316
 19961119 PCT 371 date
 19961119 PCT 102(e) date
 PRAI GB 1994-5076 19940316
 DT Utility
 FS Granted
 EXNAM Primary Examiner: Achutamurthy, Ponnathapura; Assistant Examiner: Nashed, Nashaat T.
 LREP Greenlee, Winner and Sullivan, P.C.
 CLMN Number of Claims: 19
 ECL Exemplary Claim: 1
 DRWN 24 Drawing Figure(s); 12 Drawing Page(s)
 LN.CNT 1437
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.
 AB The use of an MMP inhibitor, especially a collagenase inhibitor, in the manufacture of a medicament for the treatment of a natural or artificial tissue comprising extracellular matrix components to inhibit contraction of the tissue and methods for the treatment of tissue comprising extracellular matrix components to inhibit contraction.

L15 ANSWER 59 OF 62 USPATFULL
 AN 97:109938 USPATFULL
 TI Inhibition of TNF production with matrix metalloproteinase inhibitors
 IN Crimmin, Michael John, Cowley, Great Britain
 Galloway, William Alan, Cowley, Great Britain
 Gearing, Andrew John Hubert, Cowley, Great Britain
 PA British Biotech Pharmaceuticals Limited, Oxford, England (non-U.S. corporation)
 PI US 5691382 19971125
 WO 9410990 19940526
 AI US 1995-436190 19950512 (8)
 WO 1993-GB2331 19931112
 19950512 PCT 371 date
 19950512 PCT 102(e) date
 PRAI GB 1992-23904 19921113
 DT Utility
 FS Granted
 EXNAM Primary Examiner: Jarvis, William R. A.
 LREP Hale and Dorr LLP
 CLMN Number of Claims: 18
 ECL Exemplary Claim: 1
 DRWN No Drawings
 LN.CNT 1293
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.
 AB The present invention is directed to the method of inhibiting the release of tumor necrosis factor (TNF) in a condition mediated by TNF by administration of certain hydroxamic add derivatives, also known as matrix metalloproteinase inhibitors, and thus the method of this invention is useful in the management of diseases or conditions mediated

by TNF.

=> d his

(FILE 'HOME' ENTERED AT 14:39:37 ON 12 FEB 2003)

FILE 'REGISTRY' ENTERED AT 14:40:16 ON 12 FEB 2003

L1 1 S BATIMASTAT/CN

FILE 'CA' ENTERED AT 14:40:59 ON 12 FEB 2003

L2 167 S L1

L3 4 S 130370-60-4D

L4 167 S L2 OR L3

L5 97565 S EYE OR RETINA?

L6 9 S L5 AND L4

FILE 'WPIDS' ENTERED AT 14:44:28 ON 12 FEB 2003

L7 13 S BATIMASTAT

L8 477 S (METALLOPROTEINASE OR METALLOPROTEASE) (W) INHIBITOR

L9 54609 S EYE OR RETINAL OR RETINA

L10 24 S (L7 OR L8) AND L9

FILE 'USPATFULL' ENTERED AT 14:47:52 ON 12 FEB 2003

L11 30 S 130370-60-4/RN

L12 159 S BATIMASTAT

L13 172 S L11 OR L12

L14 162347 S EYE OR RETINA

L15 62 S L13 AND L14

L16 45932 S TOPICAL

L17 48 S L15 AND L16

=> log hold

COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
34.31	167.81

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE	TOTAL
ENTRY	SESSION
0.00	-5.58

CA SUBSCRIBER PRICE

SESSION WILL BE HELD FOR 60 MINUTES

STN INTERNATIONAL SESSION SUSPENDED AT 14:53:07 ON 12 FEB 2003

AN 97:455776 PROMT
TI Insite Vision Announces Clinical Study of Pterygium Treatment.
SO Business Wire, (20 Aug 1997) pp. 08200034.
LA English
WC 390
TX ALAMEDA, Calif.--(BW HealthWire)--Aug. 20, 1997--InSite Vision Inc. (NASDAQ:INSV) today announced a Phase II study has commenced using its ISV-120 product candidate for the prevention of recurrent pterygia, an abnormal tissue growth across the front of the eye which affects approximately four million people a year worldwide.

The study will evaluate the safety and preliminary efficacy of a three-month course of treatment with ISV-120 following surgical removal of pterygia. Up to 20 patients will be enrolled in the double-masked, placebo-controlled study. Patients will be followed for one year following surgery.

"A previous Phase II study demonstrated that ISV-120 was safe and had the potential to prevent pterygia recurrence over the 30-day dosing period," said Kumar Chandrasekaran, Ph.D., InSite Vision's chairman and chief executive officer. "By extending the treatment period from 30 days in the first trial to 90 days, we may be able to achieve long-term disease remission."

ISV-120 is a DuraSite7-based formulation of batimastat, a potent matrix metalloproteinase inhibitor which has been shown to stop the formation of blood vessels. Since pterygia are highly vascularized growths, ISV-120 may be able to stop recurrence by "starving" the pterygia of their blood source. InSite Vision obtains batimastat through a collaboration agreement with British Biotech plc.

InSite Vision is an ophthalmic pharmaceutical company focused on the development of genetically based tools for the diagnosis and prognosis of glaucoma and on the development of improved and new eye medications based on its proprietary DuraSite drug delivery platform. DuraSite-based products are designed to permit the gradual release of drug into the eye over a period of hours, thereby overcoming various treatment problems common with conventional ophthalmic drug delivery.

This press release contains, among other things, certain statements of a forward-looking nature relating to future events or the future business performance of InSite Vision Inc. Such statements involve a number of risks and uncertainties, including the results of preclinical and clinical studies and determinations by the United States Food and Drug Administration, as well as the Risk Factors listed from time to time in the company's SEC filings including, but not limited to, its report on Form 10-Q for the quarter ended June 30, 1997.

=> batimastat and retina?

L1 3 BATIMASTAT AND RETINA?

=> duplicate remove l1

DUPLICATE PREFERENCE IS 'BIOSIS, CAPLUS'
KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n

PROCESSING COMPLETED FOR L1

L2 3 DUPLICATE REMOVE L1 (0 DUPLICATES REMOVED)

ANSWER 2 OF 3 BIOSIS COPYRIGHT 2001 BIOSIS

AN 2000:251192 BIOSIS

DN PREV200000251192

TI An eye drop form of an extracellular proteinase inhibitor prevents
retinal neovascularization in an animal model.

AU Colombo, S. (1); Xu, L. (1); McGuire, P. (1); Das, A. (1)

CS (1) University of New Mexico School of Medicine, Albuquerque, NM USA

SO IOVS, (March 15, 2000) Vol. 41, No. 4, pp. S640.

Meeting Info.: Annual Meeting of the Association in Vision and
Ophthalmology. Fort Lauderdale, Florida, USA April 30-May 05, 2000
Association for Research in Vision and Ophthalmology

DT Conference

LA English

SL En